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PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

Acetaldehyde

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PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

Acetaldehyde

Environment Canada
Health Canada

May 2000

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List of Acronyms and Abbreviations

BMC	benchmark concentration
BMC_{05}	the concentration associated with a 5% increase in the benchmark endpoint
$BMCL_{05}$	the lower 95% confidence limit for the BMC_{05}
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
CEPA 1999	*Canadian Environmental Protection Act, 1999*
CFC	chlorofluorocarbon
CTV	Critical Toxicity Value
EC_{50}	median effective concentration
EEV	Estimated Exposure Value
ENEV	Estimated No-Effects Value
GWP	Global Warming Potential
K_{oc}	organic carbon/water partition coefficient
K_{ow}	octanol/water partition coefficient
kg-bw	kilogram body weight
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	Lowest-Observed-Adverse-Effect Level
LOEL	Lowest-Observed-Effect Level
MIR	maximum incremental reactivity
NAPS	National Air Pollution Surveillance
NOEL	No-Observed-Effect Level
ODP	Ozone Depletion Potential
POCP	photochemical ozone creation potential
NO_x	nitrogen oxides
PSL	Priority Substances List
TC	Tolerable Concentration
TC_{05}	Tumorigenic Concentration
TCL_{05}	lower 95% confidence limit of the TC_{05}
VOC	volatile organic compounds

SYNOPSIS

In Canada, the major use of acetaldehyde is in the production of pentaerythritol for use in alkyd resin production, fatty acid esters (synthetic lubricants), rosin and tall oil esters, and other smaller-volume applications. The Canadian domestic demand for acetaldehyde was under 10 000 tonnes in 1996.

Acetaldehyde enters the Canadian environment from natural sources (including forest and brush fires), from human sources such as fuel combustion and industrial on-site releases, and through secondary formation as a result of the atmospheric oxidation of natural and anthropogenic organic compounds. Although there are no quantitative estimates of releases from natural and secondary sources in Canada, it is believed that these sources are very large. However, the highest concentrations measured in the environment are present near anthropogenic sources. On-road motor vehicles are the largest human source of acetaldehyde emissions to the Canadian environment, releasing about 3290 tonnes per year into the air. The amount of acetaldehyde estimated to have been released into the Canadian environment from industrial processes in 1996 was 478 tonnes.

When acetaldehyde is released to or formed in air, most will undergo various degradation processes in air, and a very small amount will move into water. When acetaldehyde is released into water, it degrades there and does not move into other media. Acetaldehyde does not persist in the environment, but its continuous release and formation result in chronic exposure of biota near sources of release or formation.

Extensive recent data are available on concentrations of acetaldehyde in urban, suburban and rural air in Canada, and data are available on concentrations in air at the largest industrial emitter of acetaldehyde in Canada. Limited data are available on concentrations in surface water in four rivers and in groundwater at the industrial site that is the largest single emitter of acetaldehyde. Environmental toxicity data are available for a range of terrestrial and aquatic organisms, although mostly only for acute exposure. Based on the highest concentrations measured in air and in surface water and groundwater in Canada and on the Estimated No-Effects Values derived from experimental data for terrestrial and aquatic biota, it is unlikely that organisms are exposed to harmful levels of acetaldehyde in the Canadian ambient environment.

Acetaldehyde is not involved in the depletion of stratospheric ozone or in climate change. Because of its photo-reactivity and its moderate concentrations in the air in Canadian cities, acetaldehyde plays a role, along with other reactive volatile organic chemicals in air, in the photochemical formation of ground-level ozone.

The focus of the human health assessment is airborne exposure. Based on short-term and long-term inhalation studies conducted in experimental animals, the upper respiratory tract is the principal target site for effects of inhaled acetaldehyde. In short-term studies, acetaldehyde causes degenerative non-neoplastic effects. Although it is genotoxic both *in vitro* and *in vivo*, tumours have been observed following inhalation only at concentrations that have produced significant cytotoxicity, and it is likely that both the genotoxicity and irritancy of acetaldehyde play a role in its carcinogenicity.

Therefore, a Tolerable Concentration (based on a benchmark concentration or an Effect Level) and a Tumorigenic Concentration have been derived for this substance.

Based on the information available, it is concluded that acetaldehyde is not entering the environment in a quantity or concentration or under conditions that have or may have a

harmful effect on the environment or its biological diversity. Acetaldehyde may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends or a danger to human life or health in Canada. Therefore, acetaldehyde is considered to be "toxic" as defined in Section 64 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999).

Since acetaldehyde contributes to the formation of ground-level ozone, it is recommended that key sources of acetaldehyde be addressed as part of management plans for volatile organic chemicals associated with the formation of ground-level ozone.

Based on the comparison of the carcinogenic potency of acetaldehyde with estimates of population exposure, the priority for investigation of options to reduce exposure of the general population in the ambient environment is considered to be moderate only. Additional work on characterization of exposure of populations in the vicinity of industrial point sources and of sources in indoor air may be warranted.

1.0 INTRODUCTION

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) requires the federal Ministers of the Environment and of Health to prepare and publish a Priority Substances List (PSL) that identifies substances, including chemicals, groups of chemicals, effluents and wastes, that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" or are capable of becoming "toxic" as defined in Section 64 of the Act, which states:

> ...a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions that
> (a) have or may have an immediate or long-term harmful effect on the environment or its biological diversity;
> (b) constitute or may constitute a danger to the environment on which life depends; or
> (c) constitute or may constitute a danger in Canada to human life or health.

Substances that are assessed as "toxic" as defined in Section 64 may be placed on Schedule I of the Act and considered for possible risk management measures, such as regulations, guidelines, pollution prevention plans or codes of practice to control any aspect of their life cycle, from the research and development stage through manufacture, use, storage, transport and ultimate disposal.

Based on initial screening of readily accessible information, the rationale for assessing acetaldehyde provided by the Ministers' Expert Advisory Panel on the Second Priority Substances List (Ministers' Expert Advisory Panel, 1995) was as follows:

> This compound is used in Canada primarily in the manufacture of other chemical substances and as a finishing agent. Humans are likely to be exposed to acetaldehyde from airborne pollution. Direct human exposure may also result from other uses. Acetaldehyde is not persistent or bioaccumulative. Under laboratory conditions, it is carcinogenic when inhaled by rats and hamsters. It induces chromosome abnormalities in rodents. Information on this substance has been gathered, reviewed and evaluated by an international group of experts. An assessment is required to determine human exposure to acetaldehyde in the Canadian environment and its associated risks.

Descriptions of the approaches to assessment of the effects of Priority Substances on the environment and human health are available in published companion documents. The document entitled "Environmental Assessments of Priority Substances under the *Canadian Environmental Protection Act*, Guidance Manual Version 1.0 — March 1997" (Environment Canada, 1997a) provides guidance for conducting environmental assessments of Priority Substances in Canada. This document may be purchased from:

> Environmental Protection Publications
> Environmental Technology Advancement Directorate
> Environment Canada
> Ottawa, Ontario
> K1A 0H3

It is also available on the Internet at www.ec.gc.ca/cceb1/eng/psap.htm under the heading "Technical Guidance Manual." It should be noted that the approach outlined therein has evolved to incorporate recent developments in risk assessment methodology, which will be addressed in future releases of the guidance manual for environmental assessments of Priority Substances.

The approach to assessment of effects on human health is outlined in the following publication of the Environmental Health Directorate of Health Canada: "*Canadian Environmental Protection Act* — Human Health Risk Assessment for Priority Substances"

(Health Canada, 1994), copies of which are available from:

Environmental Health Centre
Room 104
Health Canada
Tunney's Pasture
Ottawa, Ontario
K1A 0L2

or on the Environmental Health Directorate publications web site (www.hc-sc.gc.ca/ehp/ehd/catalogue/bch.htm). The approach is also described in an article published in the *Journal of Environmental Science and Health — Environmental Carcinogenesis and Ecotoxicology Reviews* (Meek *et al.*, 1994). It should be noted that the approach outlined therein has evolved to incorporate recent developments in risk assessment methodology, which are described on the Environmental Substances Division web site (www.hc-sc.gc.ca/ehp/ehd/bch/env_contaminants/psap/psap.htm) and which will be addressed in future releases of the approach paper for the assessment of effects on human health.

The search strategies employed in the identification of data relevant to the assessment of potential effects on the environment (prior to January 1999) and human health (prior to April 1998) are presented in Appendix A. Review articles were consulted where appropriate. However, all original studies that form the basis for determining whether acetaldehyde is "toxic" under CEPA have been critically evaluated by staff of Environment Canada (entry and environmental exposure and effects) and Health Canada (human exposure and effects on human health).

Preparation of the environmental components of the assessment was led by R. Chénier with support from M. Eggleton and was coordinated by A. Bobra on behalf of Environment Canada. Sections of the Assessment Report and the supporting documentation (Environment Canada, 1999) related to the environmental assessment of acetaldehyde were prepared or reviewed by the members of the Environmental Resource Group, established by Environment Canada to support the environmental assessment:

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Environmental sections of the Assessment Report and supporting documentation (Environment Canada, 1999) were also reviewed by S. Abernethy (Ontario Ministry of the Environment), D. Ames (California Environmental Protection Agency), G. Bird (Natural Resources Canada), L. Brownlee (Environment Canada), J. Collins (California Environmental Protection Agency), A. Day (Celanese Canada Inc.), S. Dungey (United Kingdom Environment Agency), L. McCarty (L.S. McCarty Scientific Research and Consulting), G. Obe (Essen Polytechnic University), L. Seed (Health Canada) and P. Shepson (Purdue University).

The health-related sections of this Assessment Report and supporting documentation were prepared by the following staff of Health Canada:

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Sections of the supporting documentation on genotoxicity were reviewed by D. Blakey of the Environmental and Occupational Toxicology Division of Health Canada. Sections of the supporting documentation pertaining to human health were reviewed externally by R. Keefe (Imperial Oil) and C. Chopra (Bio-Tox Research Limited), primarily to address adequacy of coverage. Accuracy of reporting, adequacy of coverage and defensibility of conclusions with respect to hazard characterization and dose–response analyses were considered in written review by staff of the Information Department of BIBRA International and at a panel meeting of the following members, convened by Toxicology Excellence in Risk Assessment (TERA) on September 30, 1997, in Cincinnati, Ohio:

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A. Renwick, University of Southampton
L. Rosato, Millennium Petrochemical
L. Sirinek, Ohio Environmental Protection Agency

Helpful written comments were also received from A. Jarabek of the U.S. Environmental Protection Agency.

The health-related sections of the Assessment Report were reviewed and approved by the Health Protection Branch Risk Management meeting of Health Canada.

The entire Assessment Report was reviewed and approved by the Environment Canada/Health Canada CEPA Management Committee.

A draft of the Assessment Report was made available for a 60-day public comment period (August 14 to October 13, 1999) (Environment Canada and Health Canada, 1999). Following consideration of comments received, the Assessment Report was revised as appropriate. A summary of the comments and their responses is available on the Internet at:

www.ec.gc.ca/cceb1/eng/final/index_e.html

The text of the Assessment Report has been structured to address environmental effects initially (relevant to determination of "toxic" under Paragraphs 64(a) and (b)), followed by effects on human health (relevant to determination of "toxic" under Paragraph 64(c)).

Copies of this Assessment Report are available upon request from:

Inquiry Centre
Environment Canada
Main Floor, Place Vincent Massey
351 St. Joseph Blvd.
Hull, Quebec
K1A 0H3

or on the Internet at:

www.ec.gc.ca/cceb1/eng/final/index_e.html

Unpublished supporting documentation, which presents additional information, is available upon request from:

Commercial Chemicals Evaluation Branch
Environment Canada
14th Floor, Place Vincent Massey
351 St. Joseph Blvd.
Hull, Quebec
K1A 0H3

or

Environmental Health Centre
Room 104
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2.0 Summary of Information Critical to Assessment of "Toxic" under CEPA 1999

2.1 Identity and physical/chemical properties

Acetaldehyde is also known as ethanal, acetic aldehyde, acetylaldehyde, ethylaldehyde and methyl formaldehyde. Its Chemical Abstracts Service (CAS) registry number is 75-07-0. Acetaldehyde's empirical formula is CH_3CHO.

At room temperature, acetaldehyde is a colourless, volatile liquid with a pungent, sharp, fruity odour (CARB, 1993; IPCS, 1995). It is a highly reactive compound that undergoes numerous condensation, addition and polymerization reactions. It decomposes at temperatures above 400°C. It is highly flammable when exposed to heat or flame, and it can be explosive in air. It is miscible in all proportions with water and most common organic solvents (Hagemeyer, 1978; IPCS, 1995). In aqueous solutions, acetaldehyde exists in equilibrium with the hydrate, $CH_3CH(OH)_2$. Its degree of hydration is fairly small (1.4) (CARB, 1993). The enol form, vinyl alcohol (CH_2CHOH), exists in equilibrium with acetaldehyde to the extent of approximately 1 molecule per 30 000 (Hagemeyer, 1978; IPCS, 1995). Values for the physical and chemical properties of acetaldehyde are given in Table 1.

2.2 Entry characterization

2.2.1 Production, importation, exportation and uses

In Canada, acetaldehyde is recovered from a vinyl acetate facility, as a reactor off-gas from continuous polymerization and from the production of acetic acid by the liquid-phase oxidation of n-butane (Environment Canada, 1997c). In 1996, between 2000 and 3000 tonnes of acetaldehyde were produced in Canada. A further 6000–7000 tonnes of acetaldehyde were imported into Canada, while fewer than 10 tonnes were exported (Environment Canada, 1997c).

Acetaldehyde is used primarily as a feedstock in the production of pentaerythritol, which is used in alkyd resin production, fatty acid esters (synthetic lubricants), rosin and tall oil esters, and other smaller-volume applications (Camford Information Services, 1994; SRI International, 1995). Total Canadian consumption of acetaldehyde was reported at less than 10 000 tonnes for 1996, almost all being used for pentaerythritol production (Environment Canada, 1997c). Much smaller amounts have been used as a fragrance, deodorizer or flavouring agent, as a finishing agent, as an analytical reagent and in research and development (Environment Canada, 1996b). Acetaldehyde is also used as a feed; this use is regulated under the *Feeds Act* in Canada and is not considered further in this assessment.

2.2.2 Sources and releases

Acetaldehyde is formed and released by the combustion of organic materials and by a variety of natural processes and human activities. In addition, secondary formation of acetaldehyde occurs in the atmosphere through the oxidation of natural and anthropogenic volatile organic compounds. While there are major uncertainties associated with estimated releases from natural sources and from secondary atmospheric formation, these may be expected to be much larger than direct emissions from anthropogenic activities. However, the highest concentrations in the environment have been measured near key anthropogenic sources (see below), such as

TABLE 1 Physical and chemical properties of acetaldehyde

Property	Reported values[1]
molecular weight (g/mol)	44.05
melting point (°C)	−123.5 to −121 (−123)[2]
boiling point (°C)	20.2 to 20.8 (20.8)
vapour pressure (kPa)	98.642 to 134.018 (121.3)
water pseudo-solubility (mg/L)[3]	147,570 to 920,335 (668,000)
Henry's law constant (Pa·m³/mol)	5.423 to 10.18 (8.0)
log octanol/water partition coefficient (log K_{ow})	−0.53 to 0.52 (0.45)
log organic carbon/water partition coefficient (log K_{oc})	0.063

[1] Includes experimental and calculated values from Palit, 1947; Stull, 1947; Buttery *et al.*, 1969; Hoy, 1970; Hine and Mookerjee, 1975; Rekker, 1977; Karickhoff, 1981; Wasik *et al.*, 1981; Tewari *et al.*, 1982; Weast, 1982–83; Verschueren, 1983; Boublik *et al.*, 1984; Dean, 1985; Snider and Dawson, 1985; Leahy, 1986; Riddick *et al.*, 1986; Yoshida *et al.*, 1986; Gaffney *et al.*, 1987; Kamlet *et al.*, 1987; Betterton and Hoffmann, 1988; Nirmalakhandan and Speece, 1988; Sangster, 1989; Zhou and Mopper, 1990; Yaws *et al.*, 1991; Benkelberg *et al.*, 1995; Mackay *et al.*, 1995; DMER and AEL 1996; most values measured or calculated at 25°C and 101.3 kPa.

[2] Values in parentheses are those selected by Mackay *et al.* (1995) as being the "most reliable" data.

[3] For a substance that is fully miscible in water, a pseudo-solubility can be calculated for modelling purposes.

automotive and industrial emissions. Detailed information on sources and emission rates is discussed in Environment Canada (1999).

2.2.2.1 Natural sources

Acetaldehyde is a product of many natural processes and is naturally present in the environment. It is released during biomass combustion, such as forest and brush fires (Howard, 1990). There are no reliable estimates of amounts released from forest and brush fires, although total releases can be expected to be large. Acetaldehyde is formed by the irradiation of humic substances in water by sunlight (Kieber *et al.*, 1990).

Acetaldehyde is a metabolic intermediate in humans and other animals, in the respiration of higher plants and in alcohol fermentation (U.S. EPA, 1993; IPCS, 1995). As such, it has been found in a variety of plant and animal tissues (Collins and Bean, 1963; Furia and Bellanca, 1975; Berni and Stanley, 1982; Kami, 1983; U.S. NRC, 1985; Graedel *et al.*, 1986; Adkins *et al.*, 1990; Righetti *et al.*, 1990; Isidorov, 1992; Osborn and Young, 1993).

2.2.2.2 Anthropogenic sources

While acetaldehyde is not found in gasoline, it is a product of incomplete combustion, and all internal combustion engines have the potential to produce it. The amount generated depends primarily on the composition of the fuel, the type of engine, the emission control system, the operating temperature, and the age and state of repair of the vehicle. Therefore, release estimates are variable (see Environment Canada, 1999, for specific emission rates).

Based on the National Pollutant Release Inventory (NPRI) for 1994, on-road motor vehicles were the largest direct anthropogenic source of acetaldehyde into the environment (Environment Canada 1996a). Data on releases from on-road motor vehicles in 1994 were estimated by modelling (Mobile 5C model), using assumptions outlined in Environment Canada (1996a). It can be expected that the rates of release of acetaldehyde from automotive sources have and will continue to change; most current and planned modifications to automotive emission control technology and gasoline quality would lead to decreases in the releases of acetaldehyde

and other volatile organic compounds (VOCs), while possible increases in the use of ethanol or other oxygenated fuels could result in increases in releases of acetaldehyde (Environment Canada, 1999). The amount of acetaldehyde estimated to be released in 1994 from on-road motor vehicles in Canada was 3290 tonnes, and 677 tonnes from aircraft; other off-road gasoline-powered and diesel-powered engines also release acetaldehyde, but no reliable estimates are available. While Environment Canada (1996a) did not distinguish between gasoline-powered and diesel-powered on-road vehicles, it has been estimated, based on emission data from gasoline-powered vehicles, that the emission of acetaldehyde from gasoline-powered vehicles in 1994 was 1903 tonnes and 1387 tonnes from diesel-powered vehicles (Environment Canada, 1999).

Other anthropogenic combustion sources (covering a range of fuels from wood to plastics, polycarbonate foams and polyurethane foams) include wood-burning stoves, fireplaces, furnaces, power plants, agricultural burns, waste incinerators, cigarette smoking, coffee bean roasting and the cooking of food (Rudling *et al.*, 1981; Ramdahl *et al.*, 1982; Lipari *et al.*, 1984; MRI, 1987; Garcia *et al.*, 1992; CARB, 1993; Ryan and McCrillis, 1994; IPCS, 1995). Cigarette smoking alone in Canada is estimated to account for 5–76 tonnes per year, based on estimated emission rates (IPCS, 1995) and a Canadian consumption rate of 56 billion cigarettes per year. Canadian coal-based electricity generating plants are estimated to emit at least 28 tonnes per year, based on U.S. emission factors (Lipari *et al.*, 1984; Sverdrup *et al.*, 1994), the high heating value of fuel and Canadian coal consumption in 1995 (Rose, 1998). A gross estimate of acetaldehyde emissions from municipal, hazardous and biomedical waste in Canada is 2.6 tonnes per year, based on measured emission rates from one municipal incinerator in Ontario (Environment Canada, 1999).

Industrial releases of acetaldehyde can occur at any stage during the production, use, storage, transport or disposal of products with residual acetaldehyde. Acetaldehyde has been detected in emissions from chemical manufacturing plants (Environment Canada, 1997c), pulp and paper mills and forestry product plants (Environment Canada, 1997c; O'Connor and Voss, 1997), tire and rubber plants (Environment Canada, 1997c), petroleum refining and coal processing plants (IARC, 1985), textile mills (Kotlovoi, 1974) and food processing facilities (CARB, 1993). The total release from Canadian industry in 1996 was reported at 478 tonnes, with 69% going to air, 30% injected into deep wells and 1% released to water bodies (Environment Canada, 1997c). Acetaldehyde disposed of through deep-well injection is not considered to interact with biologically active soil strata. From 1979 to 1989, about 2.2 tonnes of acetaldehyde were reported to have been released to the environment as a result of two spills (NATES, 1996).

Acetaldehyde is a product of the degradation of sewage and solid biological wastes (U.S. EPA, 1975; Shackelford and Keith, 1976). Weschler *et al.* (1992) detected acetaldehyde released from carpets, with concentrations increasing with increasing levels of ozone. Acetaldehyde has also been detected following the exposure of interior latex paint to ozone (Reiss *et al.*, 1995).

2.2.2.3 Secondary formation

Acetaldehyde is formed in the troposphere by the photochemical oxidation of many types of organic compounds, including naturally occurring compounds (e.g., terpenes) as well as pollutants from mobile and stationary sources, such as alkenes (e.g., propene), alkanes (e.g., ethane, propane), alkylbenzenes, alcohols (e.g., allyl alcohol, ethanol, butenol, hexanol), aldehydes (e.g., propionaldehyde, acrolein), phenols, aromatic compounds, ethyl-containing compounds (e.g., ethyl peroxide) and chlorinated organics (e.g., chloroethylene, 1,1-dichloroethylene) (CARB, 1993; Grosjean *et al.*, 1993, 1994; U.S. EPA, 1993; Kao, 1994; Washington, 1995). Unlike formaldehyde, it is not produced in the atmospheric oxidation of methane and isoprene (CARB, 1993).

Given the diversity and abundance of acetaldehyde precursors in urban air, secondary atmospheric formation frequently exceeds direct emissions, especially during photochemical air pollution episodes (Grosjean *et al.*, 1983, 1993, 1994, 1996; Grosjean, 1990a,b; CARB, 1993; Harley and Cass, 1994; Washington, 1995). In California, photochemical oxidation is the largest source of acetaldehyde in the ambient air. It is estimated that it contributes between 41 and 67% of the total atmospheric acetaldehyde (CARB, 1993). Direct emissions of acetaldehyde in Los Angeles were estimated to range from 14 to 18 tonnes per day, compared with 45–180 tonnes per day for secondary formation during smog episodes (CARB, 1993). Harley and Cass (1994) also estimated that photochemical formation was more important than direct emissions in Los Angeles during the summertime days studied; in winter or at night and in the early morning, direct emissions can be more important. This was also observed in Japan, where the concentrations of acetaldehyde in the central mountainous region were not associated directly with motor exhausts but rather were associated with the photochemical oxidation of anthropogenic pollutants occurring there through long-range transport (Satsumabayashi *et al.*, 1995).

2.3 Exposure characterization

2.3.1 Environmental fate

The sections below summarize the available information on the distribution and fate of acetaldehyde released into the environment. More detailed fate information is discussed in Environment Canada (1999).

2.3.1.1 Air

Acetaldehyde emitted to air primarily reacts with photochemically generated hydroxyl (OH) radicals in the troposphere. Minor fate processes include direct photolysis and reactions with nitrate (NO_3) radicals, hydroperoxyl (HO_2) radicals and ozone (O_3). Small amounts of acetaldehyde may also transfer into rain, fog and clouds or be removed by dry deposition (Atkinson, 1989; Atkinson *et al.*, 1990, 1993; CARB, 1993).

Photo-oxidation of acetaldehyde occurs in the atmosphere through various mechanisms, such as the reaction with hydroxyl radicals, ozone, hydroperoxyl radicals and nitrate radicals. On the basis of the rate constant for each of the reactions and the concentration of the reactants, the reaction with the hydroxyl radical is considered to be the most important (Atkinson *et al.*, 1990; CARB, 1993). Factors influencing acetaldehyde's atmospheric lifetime, such as time of day, sunlight intensity and temperature, also include those affecting the availability of hydroxyl radicals and nitrate radicals. The atmospheric half-life of acetaldehyde, based on hydroxyl radical reaction rate constants, is calculated to be less than six hours (Darnell *et al.*, 1976).

Products that can be formed from photo-oxidation include peroxyacetyl nitrate, formaldehyde, peroxyacetic acid and acetic acid (Atkinson and Lloyd, 1984; Atkinson, 1989, 1990; Atkinson *et al.*, 1993). Based on data in ambient air (Grosjean, 1982; Grosjean *et al.*, 1983), acetaldehyde is one of the major precursors to peroxyacetyl nitrate formation (Atkinson *et al.*, 1990), although it contributes less than methylglyoxal and other species derived from the oxidation of aromatic compounds in urban atmospheres.

The nighttime destruction of acetaldehyde is expected to occur by the gas-phase reaction with nitrate radicals (U.S. NRC, 1981a); this tends to be more significant in urban areas, where the concentration of the nitrate radical is higher than in rural areas (Altshuller and Cohen, 1964; Gay and Bufalini, 1971; Maldotti *et al.*, 1980). A half-life of 35 days was calculated based on an average atmospheric concentration of nitrate radicals typical of a mildly polluted urban centre

(Atkinson *et al.*, 1990). Nitric acid and acetyl radicals have been identified as products of this reaction. The reaction of the nitrate radical with acetaldehyde is not therefore expected to be a significant loss process under tropospheric conditions.

Photolysis is a minor transformation pathway for acetaldehyde. The estimated half-life for photolysis is 80 hours in the lower troposphere for a zenith angle of 0°. Photolysis of acetaldehyde can take several pathways. One produces methane and carbon monoxide, while the other produces the methyl radical and formyl radical (Horowitz and Calvert, 1982; Meyrahn *et al.*, 1982; CARB, 1993). The methyl radical can react with oxygen to form the methyl peroxyl radical, which reacts with nitric oxide to form formaldehyde (U.S. EPA, 1993).

Overall half-lives for acetaldehyde in air can vary considerably under different conditions. Estimations for atmospheric residence time in several U.S. cities ranged from three hours under conditions typical of clear skies during the day in the summer to 3000 hours (125 days) under conditions typical of winter nights (U.S. EPA, 1993). During the daytime, under clear sky conditions, acetaldehyde's residence time is determined primarily by its reaction with the hydroxyl radical. Photolysis accounted for only 2–5% of the removal.

Given the generally short daytime residence times for acetaldehyde, its net atmospheric lifetimes are short. The overall half-life based on reactivity of acetaldehyde in air was estimated by Mackay *et al.* (1995) as less than 10 hours. There is therefore generally limited potential for long-range transport of this compound.

Because of its high solubility, there may be transfer of acetaldehyde into clouds and precipitation. Washout ratios (concentration in rain/concentration in air) of 28 and 37 were estimated by Atkinson (1989) at 25°C and by Buttery *et al.* (1969), respectively. Gas-phase organic compounds that are efficiently rained out have a washout ratio of greater than 10^5 (CARB, 1993). The washout ratios of acetaldehyde, together with the episodic nature of precipitation events, indicate that the wet deposition (removal of gases and particles by precipitation) of acetaldehyde is expected to be of minor significance as a tropospheric loss process (Atkinson, 1989). Benkelberg *et al.* (1995) estimated that the residence time in the atmosphere due to rain-out is 9.3 years.

2.3.1.2 Water

In water, acetaldehyde can undergo reaction with hydroxyl radicals, oxidation by alkyl or aryl peroxyl radicals, oxidation by singlet oxygen, hydration, biodegradation and volatilization (Howard, 1972; Hendry *et al.*, 1974; Foote, 1976; Mill, 1979; Buxton *et al.*, 1988; Jacob *et al.*, 1989; DMER and AEL, 1996).

Acetaldehyde should biodegrade in several days under optimal conditions (DMER and AEL, 1996). It has been degraded by various mixed cultures obtained from sludges and sewage (Ludzack and Ettinger, 1960; Thom and Agg, 1975; Speece, 1983) and by anaerobic biological treatment with unacclimatized acetate-enriched cultures (Chou and Speece, 1978). Acetaldehyde is readily biodegradable using the biodegradability test (301C) defined in the Organisation for Economic Co-operation and Development guidelines for testing of chemicals (OECD, 1992).

Biodegradation, aquatic oxidation by hydroxyl radicals and volatilization are believed to be significant environmental fate processes in water. However, acetaldehyde's residence time in water depends on the environmental conditions, such as temperature, wind speed, current, ice cover, etc. The overall reactivity-based half-life of acetaldehyde in surface water is estimated to be between 30 and 100 hours (Mackay *et al.*, 1995). No data on the half-life in groundwater were identified.

2.3.1.3 Sediment

Because of its low organic carbon/water partition coefficient (K_{oc}), acetaldehyde is not expected to significantly sorb to suspended solids and sediments in water. Biotic and abiotic degradation are expected to be the significant environmental fate processes in sediment. An overall half-life is estimated by Mackay *et al.* (1995) to be between 100 and 300 hours.

2.3.1.4 Soil

Acetaldehyde is not expected to adsorb to soil particles to a great degree and would be considered mobile in the soil, based on its estimated log K_{oc} value of 0.063. According to Kenaga (1980), compounds with a log K_{oc} of <2 are considered to be moderately mobile. Acetaldehyde can be transported to surface water through runoff and to groundwater as a result of leaching. Parameters other than K_{oc} affecting the leaching to groundwater include the soil type, the amount and frequency of rainfall, the depth of the groundwater and the extent of degradation of acetaldehyde. Acetaldehyde is susceptible to degradation (Ludzack and Ettinger, 1960; Thom and Agg, 1975; Chou and Speece, 1978; Speece, 1983).

2.3.1.5 Biota

Bioconcentration factors of 1.3 and 0.14 were calculated based on a log octanol/water partition coefficient (K_{ow}) of 0.45 (Veith *et al.*, 1980; Mackay, 1982). These values indicate that there would be little uptake or bioconcentration in aquatic organisms. Compounds with a log K_{ow} of 5 or less are generally not expected to have significant food chain build-up. No significant aquatic food chain magnification is predicted from the model calculations and empirical observations of Thomann (1989). Therefore, acetaldehyde is not expected to bioaccumulate or biomagnify.

2.3.1.6 Environmental distribution

Fugacity modelling was conducted to provide an overview of key reaction, intercompartment and advection (movement out of a system) pathways for acetaldehyde and its overall distribution in the environment. A steady-state, non-equilibrium model (Level III fugacity model) was run using the methods developed by Mackay (1991) and Mackay and Paterson (1991). Assumptions, input parameters and results are presented in Mackay *et al.* (1995) and Environment Canada (1999). This modelling assumed acetaldehyde emissions of 1000 kg/hour to air, water or soil.

Modelling indicates that when acetaldehyde is continuously discharged into a specific medium, most of it can be expected to be found in that medium, as a result of its physical-chemical properties (Mackay *et al.*, 1995; DMER and AEL, 1996; Environment Canada, 1999). More specifically, Level III fugacity modelling predicts that (Mackay *et al.*, 1995):

- when acetaldehyde is released into air, the distribution of mass is 97.1% in air, 2.6% in water, 0.3% in soil and 0.0% in sediment;
- when acetaldehyde is released into water, the distribution of mass is 0.4% in air, 99.5% in water, 0.0% in soil and 0.1% in sediment;
- when acetaldehyde is released into soil, the distribution of mass is 0.8% in air, 5.1% in water, 94.1% in soil and 0.0% in sediment.

Modelling predictions do not purport to reflect actual expected measurements in the environment but rather indicate the broad characteristics of the fate of the substance in the environment and its general distribution between media.

2.3.2 Environmental concentrations

2.3.2.1 Ambient air

Available sampling and analytical methodologies are sufficiently sensitive to detect the presence

of acetaldehyde in most samples of ambient (outdoor) air in Canada. Acetaldehyde was detected (detection limit 0.1 μg/m³) in 2798 (or 99.8%) of 2805 24-hour samples from rural, suburban and urban locations at 14 sites in six provinces surveyed from August 1989 to June 1997. Long-term (one-month to one-year) mean concentrations for these sites ranged from 0.39 to 3.35 μg/m³, with a mean concentration for all samples of 1.9 μg/m³. In urban areas in Canada, mean concentrations of acetaldehyde in 24-hour samples were generally greater than 2 μg/m³; the single highest concentration measured was 16.5 μg/m³ in Windsor, Ontario, in 1991 (Dann, 1998).

In a study in Windsor, Ontario, during 1991 and 1992, acetaldehyde was detected in all 55 samples collected, at concentrations ranging from 0.2 to 9 μg/m³; the overall mean concentration was 2.4 μg/m³ (OMEE, 1994a,b). Acetaldehyde was also detected in all 11 samples of ambient air collected during 1993 from residential and industrial areas of Hamilton, Ontario; the mean concentration was 2.1 μg/m³, with levels ranging from approximately 1.4 to 2.6 μg/m³ (Bell, 1996).

The highest concentrations of acetaldehyde in ambient air in Canada were obtained from daily monitoring data at four monitoring stations at a chemical plant. This facility is the largest reported emitter of acetaldehyde in Canada (Environment Canada, 1996a, 1997b,c). The average monthly concentrations throughout 1996 ranged from below the detection limit of 1.8 μg/m³ at some stations up to a maximum of 1150 μg/m³ at one station in July. The overall mean concentration for all stations was 199 μg/m³, with a median of 94 μg/m³ (Environment Canada, 1997c).

Average concentrations of acetaldehyde at rural Canadian sites in Nova Scotia (Tanner, 1994; Tanner *et al.*, 1994, 1996; Dann, 1998), Quebec (Dann, 1998) and Ontario (Shepson *et al.*, 1991; Dann, 1998) are generally less than or equal to 1 μg/m³. Concentrations of acetaldehyde in urban and rural areas of Canada are similar to those found in the United States and in other countries.

2.3.2.2 Indoor air

In general, concentrations of acetaldehyde in indoor air are greater than outdoor levels, due to the numerous potential indoor sources of this substance (including consumer products, cigarette smoke, combustion appliances, building materials, cooking and infiltration of vehicle exhaust) (CARB, 1996), although available data are inadequate to serve as a basis for characterization of their relative contributions. Acetaldehyde was detected in all 36 indoor air samples collected from homes in Windsor, Ontario, between 1991 and 1992 (OMEE 1994b). The mean indoor concentration (21.5 μg/m³) was considerably higher than the mean outdoor concentration (2.4 μg/m³; n = 55), with individual levels in indoor air ranging from 1.7 to 61.9 μg/m³. Acetaldehyde was detected in 11 samples of indoor air collected in 1993 from homes in residential and commercial areas of Hamilton, Ontario (Bell, 1996). The mean concentration was 15.3 μg/m³, with individual levels ranging from 3.8 to 36.3 μg/m³; the corresponding mean ambient concentration was 2.1 μg/m³ (Bell, 1996). Similar concentrations of acetaldehyde have been measured in residential indoor air studies in the United States (Highsmith *et al.*, 1988; Zhang *et al.*, 1994; Lindstrom *et al.*, 1995).

The concentration of acetaldehyde in the indoor air of office buildings is similar to that of residences. In air quality studies conducted in Canada and the United States between 1989 and 1992, mean concentrations of acetaldehyde in the indoor air of office buildings ranged from 4.1 to 16.1 μg/m³ (NIOSH, 1990; OMEE 1994b; Burt *et al.*, 1996).

Elevated levels of acetaldehyde have been measured in indoor air contaminated with environmental tobacco smoke. In monitoring studies conducted between 1987 and 1995 in Canada, the United States and the United Kingdom, mean concentrations of acetaldehyde

in indoor air contaminated with tobacco smoke ranged from 26.0 to 193.5 µg/m^3 (Lofroth *et al.*, 1989; OMEE 1994b; Williams *et al.*, 1996).

2.3.2.3 Ambient water

Anderson *et al.* (1994) measured concentrations of acetaldehyde in the raw water at three water treatment pilot plants in Ontario. The study included three distinct types of surface waters, covering a range of water parameters and regional influences: a moderately hard waterway with agricultural impacts (Grand River at Brantford), a soft, coloured river (Ottawa River at Ottawa) and a river with moderate values for most parameters, typical of the Great Lakes waterways (Detroit River at Windsor). Acetaldehyde concentrations of 114 µg/L and 1.4 µg/L were measured in samples collected on December 2, 1993, and on February 15, 1994, from the Detroit River. In the Ottawa River, concentrations were below the detection limit (0.9 µg/L) in three profiles taken between April 12 and June 7, 1994. A concentration of 5.9 µg/L was measured on December 9, 1993. No acetaldehyde was detected (0.9 µg/L) on seven sampling dates between May 11 and July 21, 1994, in the Grand River.

Concentrations of acetaldehyde in raw water from the North Saskatchewan River were measured at a drinking water pilot plant in Edmonton, Alberta. Concentrations between March 1989 and January 1990 averaged 8 µg/L, with a peak value of 31 µg/L. These concentrations were influenced by climatological events, as evidenced by an increase in concentrations during spring runoff and major rainfall and a reduction in concentrations (<0.7 µg/L) following river freeze-up (Huck *et al.*, 1990).

Monitoring data for groundwater at the site of the largest known industrial emitter of acetaldehyde in Canada included nine samples in which acetaldehyde concentrations were below the detection limit (50 µg/L) and four samples with measurable concentrations (140, 370, 1200 and 1300 µg/L) (Environment Canada, 1997c).

While no data are available in Canada, concentrations of acetaldehyde in rain, fog, cloud water and snow have been measured in other countries. Concentrations ranged from below detection to 190 µg/L for snow, from 1.3 to 100 µg/L for rain, from 220 to 1100 µg/L for fog water and from below detection to 2400 µg/L (over Los Angeles, California) for cloud water (see Environment Canada, 1999).

2.3.2.4 Drinking water

Data concerning measured levels of acetaldehyde in drinking water in Canada are limited to two investigations conducted at pilot-scale surface water treatment facilities in Alberta and Ontario. In an unspecified number of samples of treated drinking water collected from March 1989 to January 1990 at a treatment plant in Edmonton, Alberta, mean concentrations of acetaldehyde in finished water ranged from 5.5 to 6.3 µg/L (Huck *et al.*, 1990). In a pilot study of Ontario treatment plants located in Ottawa, Brantford and Windsor conducted between 1993 and 1994, reported concentrations of acetaldehyde in finished drinking water ranged from not detected (i.e., <0.9 µg/L) to 20 µg/L (Anderson *et al.*, 1994).

In a study conducted in the United States, acetaldehyde was not detected (i.e., <1.0 µg/L) in six samples of finished drinking water collected at Freemont, California (Wu and White, 1995). Krasner *et al.* (1989) reported median concentrations of acetaldehyde ranging from 2.1 to 6.1 µg/L in 24 samples of treated drinking water collected in 1989 from eight water treatment facilities in the United States. Concentrations of acetaldehyde ranged from not detected (detection limit 1.1 µg/L) to 9.5 µg/L in an unspecified number of samples of finished drinking water collected in July 1988 at one groundwater and one surface water treatment facility in southern California (Glaze *et al.*, 1989). In studies conducted at a surface water treatment facility in Turin, Italy, during 1988, acetaldehyde was detected in 83% of finished drinking water samples at a mean concentration of 0.5 µg/L (Gilli *et al.*, 1989).

2.3.2.5 Sediment and soil

No data on measured concentrations of acetaldehyde in sediments or in soils in Canada were identified.

2.3.2.6 Biota

Data on concentrations of acetaldehyde in Canadian biota were not identified.

2.3.2.7 Food

No data were identified concerning the concentrations of acetaldehyde in foodstuffs consumed in Canada; however, acetaldehyde is a natural component of many foods (Feron *et al.*, 1991) and is generated during the ripening of fruit (Bartley and Schwede, 1989), during cooking and baking (Lorenz and Maga, 1972; Yasuhara and Shibamoto, 1995) and during the storage and maturation of alcoholic beverages (Jones *et al.*, 1986). Acetaldehyde is generally recognized as safe (GRAS) in the United States and is used in Canada and the United States as a synthetic flavouring substance and adjuvant in various foods (including dairy and meat products, fruit juices, baked goods, alcoholic and non-alcoholic beverages, gelatin desserts and candy). Reported concentrations of acetaldehyde in these products have ranged from 3.9 mg/L in beverages to 2000 µg/g in frosting (U.S. FDA, 1982; U.S. NRC, 1985; Burdock, 1995; Feeley, 1996). In a review of the occurrence of acetaldehyde in various foods, Maarse and Visscher (1992) reported concentrations of acetaldehyde ranging from 0.2 to 230 µg/g in fruit and fruit juices (including apples, pears, strawberries, apple juice, orange juice and grapefruit juice), from 0.2 to 400 µg/g in vegetables (cabbage, carrots, celery, cucumber, peas, beans, corn and tomatoes) and from 4.2 to 9.9 µg/g in bread. Reported concentrations of acetaldehyde in dairy products (milk, cheese, cream and yogurt) and fats (butter) have ranged from 0.001 to 76.0 µg/g (Maarse and Visscher, 1992; Miyake and Shibamoto, 1993), while concentrations in seafood, meat, eggs and nuts have ranged from 0.001 to 2.7 µg/g (Halvarson, 1972; Maarse and Visscher, 1992). Measured concentrations of acetaldehyde in non-alcoholic beverages are low, with levels in tea and soft drinks ranging from 0.2 to 0.6 µg/g (Maarse and Visscher, 1992; Miyake and Shibamoto, 1993).

Acetaldehyde is produced as an intermediate during alcoholic fermentation and as an unwanted product during the storage and maturation of alcoholic products, imparting an unpleasant taste (Geiger and Piendl, 1976; Hagemeyer, 1978; Jones *et al.*, 1986). Based on reported concentrations of acetaldehyde in three brands of beer from the United States (Miyake and Shibamoto, 1993), 18 commercial brands of beer purchased in Europe (Delcour *et al.*, 1982) and an unspecified number of samples of beer in the study by Maarse and Visscher (1992), concentrations of acetaldehyde in beer have ranged from 0.6 to 24 µg/g. Based on available data, concentrations of acetaldehyde in wine are highly variable, with measured levels ranging from 0.7 to 290 µg/g (Okamoto *et al.*, 1981; Maarse and Visscher, 1992). Similarly, concentrations of acetaldehyde in other alcoholic products (including rum, whiskey, brandy, gin, cognac and sake) are highly variable, with reported levels ranging from 0.5 to 104 µg/g (Maarse and Visscher, 1992; Miyake and Shibamoto, 1993).

Identified information concerning the concentration of acetaldehyde in breast milk is limited to one study in which this substance was detected (limit of detection not reported) but not quantified in four of 12 samples of breast milk collected from 12 women at four urban locations (Bridgeville, Pennsylvania; Bayonne, New Jersey; Jersey City, New Jersey; and Baton Rouge, Louisiana) in the United States (Pellizzari *et al.*, 1982).

2.4 Effects characterization

2.4.1 Ecotoxicology

There exist several toxicity studies on acetaldehyde due to its wide use in many applications. Below, a brief summary is presented of the most sensitive endpoints found for terrestrial and aquatic organisms. More extensive descriptions of environmental effects are provided in Environment Canada (1999).

2.4.1.1 Terrestrial organisms

While no data on the toxicity of acetaldehyde to terrestrial vertebrate wildlife were identified in the literature, data are available from mammalian toxicology studies (Section 2.4.3). No data were found on avian toxicity.

Acetaldehyde has been shown to be an effective fumigant to control a broad range of bacteria, moulds, yeasts and thrips associated with fruit spoilage (Aharoni and Barkai-Golan, 1973; Aharoni and Stadelbacher, 1973; U.S. NRC, 1981b; Avissar *et al.*, 1990; Yuen *et al.*, 1995). Effect concentrations range from 540 to 357 000 mg/m^3 for 11 species of fungi. The most sensitive response identified was a 95% and 91% reduction in fruit decay by *Penicillium italicum* and *P. digitatum*, respectively, after a five-day exposure to acetaldehyde vapour at 540 mg/m^3 (0.03% v/v) (Yuen *et al.*, 1995).

Invertebrates appear less sensitive than fungi, with reported effect concentrations ranging from 4500 to 36 000 mg/m^3 in air for five species of developing and adult insects and slugs (Burditt *et al.*, 1963; Henderson, 1970; Aharoni *et al.*, 1979; Stewart *et al.*, 1980; Rohitha *et al.*, 1993). The most sensitive species tested was the aphid, *Acythosiphon kondai*, with 100% mortality at all life stages when exposed to 4500 mg acetaldehyde/m^3 (Aharoni *et al.*, 1979).

While toxicity data for terrestrial plants are limited, plants are less sensitive than fungi to acetaldehyde. Acetaldehyde concentrations of 54 000–108 000 mg/m^3 for four hours caused dark-green, water-soaked, necrotic areas on the outer leaves of head lettuce (*Lactuca sativa*). Fumigation with up to 36 000 mg/m^3 did not cause injury to the lettuce (Aharoni *et al.*, 1979; Stewart *et al.*, 1980).

2.4.1.2 Aquatic organisms

Almost all data identified for aquatic organisms were from short-term studies.

The most sensitive aquatic species identified is the fathead minnow (*Pimephales promelas*). A flow-through test was done at 24°C with 30-day-old fish and duplicate exposures. Based on measured concentrations of acetaldehyde, the 96-hour LC_{50} was 30.8 mg/L (95% confidence interval 28.0–34.0 mg/L) (Brooke *et al.*, 1984). Other short-term LC_{50} values for fish, including the guppy (*Poecilia reticulata*), the pinfish (*Lagodon rhomboides*) and the bluegill (*Lepomis macrochirus*), range from 33 to 140 mg/L (Daugherty and Garrett, 1951; Juhnke and Luedemann, 1978; Grahl, 1983; Deneer *et al.*, 1988; Geiger *et al.*, 1990; Nendza and Russom, 1991; Von Burg and Stout, 1991).

Aquatic invertebrates are similarly sensitive to acetaldehyde. The lowest value identified was a 48-hour EC_{50} (immobilization; static conditions) of 42 mg/L reported for the water flea, *Daphnia magna* (Von Burg and Stout, 1991). Other short-term effect concentrations (EC_{50}s, LC_{50}s) range up to 14 221 mg/L for species including the water flea, *Ceriodaphnia dubia*, the common shrimp (*Crangon crangon*) and the pond snail (*Lymnaea stagnalis*) (Portmann and Wilson, 1971; Randall and Knopp, 1980; Takahashi *et al.*, 1987; Mills *et al.*, 1990).

For microorganisms, the most sensitive effect of acetaldehyde reported is for the protozoan, *Chilomonas paramecium*, with a a 48-hour EC_{50} (population growth) of 82 mg/L (Von Burg and Stout, 1991). Five-day LC_{50}s for the diatom, *Nitzchia linearis*, range from 237 to 249 mg/L (Patrick *et al.*, 1968). A 25-minute EC_{50}

of 303 mg/L was reported for *Photobacterium phosphoreum* in a Microtox test (Chou and Que Hee, 1992). Blue-green algae (*Anabaena* sp. and *Nostoc* sp.) have 10- to 14-day EC_{50}s (growth) of 4528–16 244 mg/L (Stratton, 1987).

2.4.2 *Abiotic atmospheric effects*

The potential for acetaldehyde to contribute to the depletion of stratospheric ozone, to climate change and to formation of ground-level ozone was examined.

Since acetaldehyde is not a halogenated compound, its Ozone Depletion Potential (ODP) is 0, and it will therefore not contribute to the depletion of stratospheric ozone (Bunce, 1996).

Gases involved in climate change strongly absorb infrared radiation of wavelengths between 7 and 13 µm, enabling them to trap and re-radiate the Earth's thermal radiation (Wang *et al.*, 1976; Ramanathan *et al.*, 1985). Worst-case calculations were made to determine if acetaldehyde has the potential to contribute to climate change (Bunce, 1996), assuming it has the same infrared absorption strength as the reference compound CFC-11. The Global Warming Potential (GWP) was calculated to be 1.3×10^{-4} (relative to the reference compound CFC-11, which has a GWP of 1), based on the following formula:

$$GWP = (t_{acetaldehyde}/t_{CFC-11}) \times (M_{CFC-11}/M_{acetaldehyde}) \times (S_{acetaldehyde}/S_{CFC-11})$$

where:

- $t_{acetaldehyde}$ is the lifetime of acetaldehyde (2.4×10^{-3} years),
- t_{CFC-11} is the lifetime of CFC-11 (60 years),
- M_{CFC-11} is the molecular weight of CFC-11 (137.5 g/mol),
- $M_{acetaldehyde}$ is the molecular weight of acetaldehyde (44 g/mol),
- $S_{acetaldehyde}$ is the infrared absorption strength of acetaldehyde (2389/cm^2 per atmosphere, default), and
- S_{CFC-11} is the infrared absorption strength of CFC-11 (2389/cm^2 per atmosphere).

Since this estimate for the GWP is much less than 1% of that of the reference compound, acetaldehyde is not considered to be involved in climate change (Bunce, 1996).

The contribution of VOCs to the formation of ground-level ozone and the resulting contribution to smog formation is a complex process and has been studied extensively. The terms reactivity, incremental reactivity and photochemical ozone formation potential denote the ability of an organic compound in the atmosphere to influence the formation of ozone (Paraskevopoulos *et al.*, 1995). Estimates of reactivity of a substance depend on the definition and method of calculation of the reactivity, the VOC/NO_x ratio, the age of the air mass, the chemical mechanisms in the model, the chemical composition of the hydrocarbon mixture into which the VOC is emitted, the geographical and meteorological conditions of the airshed of interest (including temperature and intensity and quality of light), and the extent of dilution (Paraskevopoulos *et al.*, 1995).

The Photochemical Ozone Creation Potential (POCP) is one of the simpler indices of the potential contribution of an organic compound to the formation of ground-level ozone, based on the rate of reaction of the substance with the hydroxyl radical relative to ethene (CEU, 1995). Ethene, a chemical that is considered to be important in ozone formation, has an assigned POCP value of 100. The POCP for acetaldehyde was estimated to be 121 relative to ethene, using the following formula (Bunce, 1996):

$$POCP = (k_{acetaldehyde}/k_{ethene}) \times (M_{ethene}/M_{acetaldehyde}) \times 100$$

where:

- $k_{acetaldehyde}$ is the rate constant for the reaction of acetaldehyde with OH radicals (1.62×10^{-11} cm^3/mol per second),

- k_{ethene} is the rate constant for the reaction of ethene with OH radicals (8.5×10^{-12} cm^3/mol per second),
- M_{ethene} is the molecular weight of ethene (28.1 g/mol), and
- $M_{acetaldehyde}$ is the molecular weight of acetaldehyde (44.1 g/mol).

Various published reactivity values for acetaldehyde and other selected VOCs are presented by Paraskevopoulos *et al.* (1995). The use of a maximum incremental reactivity (MIR) scale has been recommended by Carter (1994) as optimal when applied to the wide variety of conditions where ozone is sensitive to VOCs, being fairly robust to the choices of scenarios used to derive it. Experimental data indicate that for acetaldehyde, direct radical formation from its photolysis is the key factor leading to net contribution to ozone formation under conditions of low reactive organic gas to NO_x ratios (Carter *et al.*, 1995).

Recently, acetaldehyde was one of the VOCs identified in the Canadian 1996 NO_x/VOC Science Assessment as part of the Multi-Stakeholder NO_x/VOC Science Program (Dann and Summers, 1997). Based on air measurements taken at nine urban and suburban sites in Canada from June to August from 1989 to 1993, acetaldehyde was ranked 22nd of the most abundant non-methane hydrocarbon and carbonyl species. Based on these measurements and on a maximum incremental reactivity (MIR) value of 2.56 mol ozone/mol carbon, acetaldehyde represented approximately 3.4% of the total volatile organic carbon reactivity and was ranked 8th when sorted by the total volatile organic carbon reactivities. Total volatile organic carbon reactivity denotes the ability of organic compounds to contribute to the formation of ozone.

Therefore, based on its reactivity and the concentrations encountered in Canada, acetaldehyde is likely to play a role in the photochemical formation of ground-level ozone in urban areas in Canada.

2.4.3 *Experimental animals and* in vitro

2.4.3.1 Acute toxicity

The acute toxicity of acetaldehyde is low, with LC_{50}s for 30-minute or four-hour inhalation exposures ranging from 24 to 37 g/m³, and LD_{50}s for oral administration ranging from >600 to 1930 mg/kg-bw. Principal signs of acute toxicity are central nervous system depression, reduced respiratory rate, increased heart rate and blood pressure, pulmonary edema and albuminuria.

2.4.3.2 Irritation and sensitization

No data were identified concerning the potential of acetaldehyde to induce sensitization in experimental animals. Acetaldehyde is irritating to the skin, eyes and upper respiratory tract in inhalation studies and has been shown to induce sensory irritation in rodents (U.S. NRC, 1977; Steinhagen and Barrow, 1984; Babiuk *et al.*, 1985; U.S. EPA, 1987; ITII, 1988; Cassee *et al.*, 1996b).

2.4.3.3 Short-term and subchronic toxicity

2.4.3.3.1 Inhalation

In the study with optimum characterization of concentration–response, Wistar rats exposed to 400, 1000, 2200 or 5000 ppm (720, 1800, 3960 or 9000 mg/m³) acetaldehyde for six hours per day, five days per week, for four weeks had concentration-related histopathological changes in the nasal olfactory and respiratory epithelium (including thinning and disarrangement of epithelial cells, loss of microvilli and sensory cells, focal hyperplasia, stratified squamous metaplasia and keratinization) (Appelman *et al.*, 1982). [Lowest-Observed-Effect Level (LOEL) = 400 ppm (720 mg/m3)]

In subsequent studies, male SPF Wistar rats were exposed to acetaldehyde for six hours per day, five days per week, for four weeks in three different exposure regimens: as a single daily exposure to 0, 150 or 500 ppm (0, 270 or

900 mg/m³); as two daily three-hour exposures to 0, 150 or 500 ppm (0, 270 or 900 mg/m³) with an intervening 1.5-hour resting period; or as two daily three-hour exposures to 0, 110, 150 or 500 ppm (0, 198, 270 or 900 mg/m³) with a 1.5-hour period of eight five-minute peak exposures to 0, 660 or 3000 ppm (six-hour time-weighted average = 0, 270 or 1050 mg/m³) (Appelman *et al.*, 1986). Compared with controls, no effects were observed among rats exposed (intermittently or continuously) to 110 or 150 ppm (198 or 270 mg/m³) acetaldehyde for six hours per day, even when combined with additional (cytotoxic) exposures to 660 or 3000 ppm (six-hour time-weighted average = 270 or 1050 mg/m³) acetaldehyde. In male rats exposed to 500 ppm (900 mg/m³) acetaldehyde for six hours per day, five days per week, for four weeks, there were slight histopathological changes (i.e., loss of microvilli and disarrangement of the epithelium) in the olfactory epithelium and a reduction in the phagocytic index of lung macrophages. Variation in the pattern of exposure to include a 1.5-hour resting period did not significantly alter the observed histopathological changes in the nose or the phagocytic index. Intermittent exposure to concentrations up to 3000 ppm (six-hour time-weighted average = 1050 mg/m³) acetaldehyde for 1.5 hours, in addition to the initial exposure to 500 ppm (900 mg/m³) acetaldehyde for six hours per day, resulted in significant growth retardation, slight irritation and a further reduction of the phagocytic index, while there was no change in the severity of the histopathological changes observed in the nasal epithelium, compared with rats exposed only to 500 ppm (900 mg/m³) acetaldehyde for six hours per day (Appelman *et al.*, 1986). [No-Observed-Effect Level (NOEL) = 150 ppm (270 mg/m³); LOEL = 500 ppm (900 mg/m³)]

In other short-term inhalation studies, in which only a limited range of endpoints was examined in rats and mice, histopathological changes in the nasal olfactory epithelia and functional changes in the lungs (in rats) were observed at concentrations as low as 243 ppm (437 mg/m³) acetaldehyde (Watanabe and Aviado, 1974; Saldiva *et al.*, 1985; Cassee *et al.*, 1996a). [Lowest-Observed-Adverse-Effect Level (LOAEL) = 243 ppm (437 mg/m³)]

In the only subchronic inhalation study identified, Syrian golden hamsters exposed by inhalation to 390, 1340 or 4560 ppm (702, 2412 or 8208 mg/m³) acetaldehyde for six hours per day, five days per week, for 13 weeks had organ weight changes (ovary and kidney) and concentration-related histopathological changes in the trachea at 1340 ppm (2412 mg/m³) acetaldehyde and higher (Kruysse *et al.*, 1975). [NOEL = 390 ppm (702 mg/m³); LOAEL = 1340 ppm (2412 mg/m³)]

2.4.3.3.2 Ingestion

In short-term studies in which a wide range of endpoints was examined, focal hyperkeratosis of the forestomach, increased relative kidney weights and alterations in clinical chemistry parameters were observed in Wistar rats receiving 675 mg acetaldehyde/kg-bw per day in drinking water for four weeks (Til *et al.*, 1988). [NOEL = 125 mg/kg-bw per day; LOAEL = 675 mg/kg-bw per day]

In the only subchronic investigation identified, in which only overt toxicity, body weight gain and hepatic effects were considered, histopathological effects in the liver (including microvesicular fatty degeneration, fatty accumulation and foci of inflammatory cells) were observed among rats receiving 500 mg acetaldehyde/kg-bw per day in drinking water (Matysiak-Budnik *et al.*, 1996). [NOEL = 120 mg/kg-bw per day; LOAEL = 500 mg/kg-bw per day]

2.4.3.4 Chronic toxicity and carcinogenicity

In the only chronic inhalation study of adequate design, Wistar rats (both sexes) were exposed by inhalation to 750, 1500 or 3000 ppm (1350, 2700 or 5400 mg/m³) acetaldehyde for six hours per day, five days per week, for up to 28 months (due to early mortality and severe growth retardation, the highest concentration was reduced from 3000 ppm [5400 mg/m³] in week 20 to

1000 ppm [1800 mg/m^3] in week 52 and beyond) (Woutersen *et al.*, 1984, 1986; Feron *et al.*, 1985; Woutersen and Feron, 1987). Compared with unexposed controls, exposure to acetaldehyde produced histopathological changes (i.e., focal basal cell hyperplasia, aggregates of atypical cells and proliferation) in the nasal olfactory epithelium of both sexes at all levels of exposure. The inclusion of a 26- or 52-week recovery period following exposure to acetaldehyde for 52 weeks resulted in some regeneration of the nasal olfactory epithelium among animals (particularly females) exposed to 750 or 1500 ppm (1350 or 2700 mg/m^3) acetaldehyde, but not among animals exposed to higher concentrations (Woutersen and Feron, 1987). [LOAEL (non-neoplastic histopathological effects in the upper respiratory tract of males and females) = 750 ppm (1350 mg/m^3)]

Compared with controls, there was a significant (concentration-related) increase in the incidence of nasal carcinomas (derived principally from respiratory epithelia) and adenocarcinomas (derived principally from olfactory epithelia) among males and females exposed to acetaldehyde for 52 weeks or 28 months (Woutersen *et al.*, 1984, 1986; Woutersen and Feron, 1987). At 28 months, the incidence of nasal squamous cell carcinomas in male rats exposed to 0, 750, 1500 or 3000/1000 ppm (0, 1350, 2700 or 5400/1800 mg/m^3) acetaldehyde was 1/49, 1/52, 10/53 ($p < 0.05$) and 15/49 ($p < 0.001$), respectively; the incidence in females was 0/50, 0/48, 5/53 and 17/53 ($p < 0.001$), respectively. At 28 months, the incidence of nasal adenocarcinomas in male rats exposed to 0, 750, 1500 or 3000/1000 ppm (0, 1350, 2700 or 5400/1800 mg/m^3) acetaldehyde was 0/49, 16/52 ($p < 0.001$), 31/53 ($p < 0.001$) and 21/49 ($p < 0.001$), respectively; the incidence in females was 0/50, 6/48 ($p < 0.05$), 26/53 ($p < 0.001$) and 21/53 ($p < 0.001$), respectively. The incidence of carcinoma *in situ* in the nasal cavity of rats was not statistically significant. No exposure-related neoplastic lesions were observed in other major tissues and organs examined (Woutersen *et al.*, 1984, 1986; Woutersen and Feron, 1987).

Acetaldehyde did not induce tumours in male Syrian golden hamsters exposed by inhalation (whole body) to a single concentration of 1500 ppm (2700 mg/m^3) acetaldehyde for seven hours per day, five days per week, for 52 weeks (Feron, 1979). However, exposure produced (reversible) non-neoplastic lesions in the dorsal area of the nasal cavity and trachea, a reduction in growth, alterations in hematological and urinary parameters, and increased relative kidney weights, compared with controls (Feron, 1979). [LOAEL for non-neoplastic effects = 1500 ppm (2700 mg/m^3); single exposure level]

In a subsequent study in which Syrian golden hamsters were exposed to a single concentration of 2500 ppm (4500 mg/m^3) acetaldehyde (reduced to 1650 ppm [2970 mg/m^3] due to extensive growth retardation) for seven hours per day, five days per week, for 52 weeks, followed by a 29-week recovery period, exposure produced a reduction in growth and non-neoplastic histopathological lesions in the nasal cavities, larynx and trachea, compared with unexposed controls (Feron *et al.*, 1982). No tumours were observed among surviving animals sacrificed after 52 weeks of exposure, while an increase ($p < 0.05$) in the incidence of laryngeal tumours (including poly/papilloma, carcinoma *in situ*, squamous cell carcinoma and adeno-squamous carcinoma) was observed among animals exposed to acetaldehyde and found dead or moribund; the (combined) incidence of these tumours in males and females was 26% (6/23) and 20% (4/20), respectively, while no tumours were observed among controls. In addition, animals exposed to acetaldehyde and found dead or moribund had tumours in the nasal cavities, including adenomas, adenocarcinomas and anaplastic carcinomas; however, the incidence of these tumours was not statistically significant (Feron *et al.*, 1982). [LOAEL for non-neoplastic effects = 2500/1650 ppm (4500/2970 mg/m^3); single exposure level]

No exposure-related tumours were observed in Syrian golden hamsters (both sexes) administered weekly intratracheal instillations of acetaldehyde (approximately 30 or 60 mg

acetaldehyde/kg-bw per week) for 52 weeks, while exposure produced extensive non-neoplastic changes in the lung of males and females (including peribronchiolar adenomatoid lesions and inflammation of the bronchoalveolar region), compared with saline controls (Feron, 1979; Feron *et al.*, 1982).

Studies concerning the effects of chronic ingestion of acetaldehyde in laboratory animals have not been identified.

2.4.3.5 Genotoxicity

In *in vitro* studies, acetaldehyde was mutagenic in mammalian cells (Wangenheim and Bolcsfoldi, 1986, 1988; He and Lambert, 1990), induced aneuploidy in *Saccharomyces cerevisiae* (Albertini *et al.*, 1993; Ristow *et al.*, 1995), Chinese hamster embryo cells and rat skin fibroblasts, and increased the frequency of micronuclei in rat skin fibroblasts and human lymphocytes (Bird *et al.*, 1982; Dulout and Furnus, 1988; Migliore and Nieri, 1991). Acetaldehyde induced structural chromosomal aberrations in Chinese hamster cells (Au and Badr, 1979; Dulout and Furnus, 1988) and rat skin fibroblasts (Bird *et al.*, 1982), while results have been mixed in human lymphocytes (Badr and Hussain, 1977; Obe *et al.*, 1979). Positive results were observed for sister chromatid exchange in Chinese hamster ovary cells (Obe and Ristow, 1977; Obe and Beek, 1979; DeRaat *et al.*, 1983; Brambilla *et al.*, 1986), human lymphocytes (Ristow and Obe, 1978; Jansson, 1982; Bohlke *et al.*, 1983; He and Lambert, 1985; Knadle, 1985; Norppa *et al.*, 1985; Obe *et al.*, 1986; Lambert and He, 1988; Helander and Lindahl-Kiessling, 1991; Sipi *et al.*, 1992) and pre-implantation mouse embryos (Lau *et al.*, 1991). Acetaldehyde also induced unscheduled DNA synthesis in rat hepatocytes (Stevens *et al.*, 1991) and DNA cross-linking in Chinese hamster ovary cells (Marinari *et al.*, 1984; Olin *et al.*, 1996), *Escherichia coli* plasmid DNA (Kuykendall and Bogdanffy, 1992a,b), calf thymus DNA (Sillanaukee *et al.*, 1991) and homogenates of rat nasal mucosa (Lam *et al.*, 1986; Kuykendall *et al.*, 1993).

In *in vivo* studies (conducted by intraperitoneal injection), acetaldehyde induced sister chromatid exchange in the bone marrow cells of hamsters and mice and increased the frequency of micronuclei in the erythrocytes of mice (Obe *et al.*, 1979; Korte and Obe, 1981; Ma *et al.*, 1985). Acetaldehyde also increased the frequency of chromosomal aberrations in rat embryos exposed by intra-amniotic injection (Barilyak and Kozachuk, 1983) and induced recessive lethal mutations in *Drosophila melanogaster* (Woodruff *et al.*, 1985) and gene mutation in *Caenorhabditis elegans* (Greenwald and Horvitz, 1980).

The results of *in vivo* studies suggest that acetaldehyde can react directly with DNA and proteins to form stable adducts. Acetaldehyde produced a concentration-related reduction in the extractability of DNA (suggestive of increased formation of DNA–protein cross-links) from the respiratory nasal mucosa of Fischer 344 rats exposed (whole body) to 1000 or 3000 ppm (1800 or 5400 mg/m^3) acetaldehyde for six hours or to 1000 ppm (1800 mg/m^3) acetaldehyde for six hours per day for five days. Significant reduction in the extractability of DNA in the nasal olfactory epithelia was observed only following exposure to 1000 ppm (1800 mg/m^3) acetaldehyde for six hours per day for five days (Lam *et al.*, 1986).

2.4.3.6 Reproductive and developmental toxicity

Data concerning the reproductive effects of *in vivo* administration of acetaldehyde (conducted using physiologically relevant routes of exposure) are limited to the results of one subchronic investigation in which an assessment of ovary weights, testicular weights and other testicular parameters was conducted in hamsters exposed by inhalation. Based on the results of this study, reduced gonad weights have been observed at 1340 ppm (2412 mg/m^3) acetaldehyde and higher (Kruysse *et al.*, 1975).

In identified *in vivo* studies concerning the developmental toxicity of acetaldehyde, dose-related embryotoxic, fetotoxic and/or teratogenic effects have been observed (O'Shea and Kaufman, 1979; Sreenathan *et al.*, 1982, 1984a,b; Barilyak and Kozachuk, 1983; Padmanabhan *et al.*, 1983; Webster *et al.*, 1983; Blakely and Scott, 1984; Checiu *et al.*, 1984; Schreiner *et al.*, 1987; Ali and Persaud, 1988; Fadel and Persaud, 1990, 1993). However, in each of these investigations, the dams were exposed by non-physiological routes of administration, primarily because the studies were designed to investigate the effects of acetaldehyde produced as a metabolite of alcohol; moreover, maternal toxicity was not adequately assessed or reported.

2.4.3.7 Neurological effects and effects on the immune system

Although data are limited, results of available toxicity studies conducted (via inhalation) in rodents do not indicate that neurological or immunological effects are critical endpoints associated with exposure to acetaldehyde; i.e., such effects were not observed at concentrations lower than those that induced damage in the respiratory tract (Ortiz *et al.*, 1974; Shiohara *et al.*, 1985; Aranyi *et al.*, 1986; Roumec *et al.*, 1988).

2.4.3.8 Toxicokinetics and mechanism of action

Small amounts of acetaldehyde are produced endogenously during the normal intermediary catabolism of deoxyribose phosphate and various amino acids (Nicholls *et al.*, 1992; Jones, 1995). Consumption of alcoholic beverages is also an important source of acetaldehyde in the body, formed through the metabolism of ethanol by alcohol dehydrogenase.

Consistent with effects being observed primarily at the initial site of exposure following inhalation (i.e., in the respiratory tract), available data indicate that the greatest proportion of inhaled acetaldehyde is retained at the site of contact, becoming rapidly and irreversibly bound to free protein and non-protein sulphydryl groups (notably, cysteine and glutathione). The results of pharmacokinetic studies conducted in humans (Dalhamn *et al.*, 1968; Egle, 1970) and rodents (David and Heck, 1983; Morris, 1997) indicate that the absorption of acetaldehyde into the systemic circulation is likely not extensive following inhalation. Based on the high degree of retention of acetaldehyde in the respiratory tract following inhalation in humans, it is likely that the predominant pathway for the metabolism of acetaldehyde involves conjugation to thiols (i.e., cysteine and glutathione) at the site of exposure, subsequent formation of hemimercaptal or thiazolidine intermediates, and elimination of thioethers and disulphides in the urine (Sprince *et al.*, 1974; Cederbaum and Rubin, 1976; Hemminiki, 1982; Brien and Loomis, 1983; Nicholls *et al.*, 1992). Inhaled acetaldehyde is also rapidly oxidized (to acetate) by aldehyde dehydrogenase in human nasal and lung epithelia (Bogdanffy *et al.*, 1986; Yin *et al.*, 1992; Morris *et al.*, 1996).

Many of the toxicological effects of acetaldehyde may be due to the saturation of protective cellular mechanisms at the initial site of exposure. As with formaldehyde, the potential for acetaldehyde to react with epithelial DNA (and other cellular components) in the upper respiratory tract may be dependent upon the levels of intracellular thiols (notably glutathione and cysteine), which prevent binding of acetaldehyde with critical sulphydryl groups in proteins, peptides and DNA (Cederbaum and Rubin, 1976; U.S. EPA, 1987; von Wartburg, 1987). In addition, regional deficiencies in aldehyde dehydrogenase activity in rats correlate with the distribution of nasal lesions in another strain of rats exposed to acetaldehyde in inhalation studies (Bogdanffy *et al.*, 1986). Observed decreases in uptake of acetaldehyde at high concentrations (>100 ppm [>180 mg/m^3]) in a range of species may be a function of exceedance of the metabolic capacity of nasal aldehyde dehydrogenase (Morris, 1997).

The pattern of observed irritancy of acetaldehyde at the site of contact and the results of studies indicating that it can react directly

with DNA and proteins to form stable adducts is similar to that for other aldehydes (such as formaldehyde) that have been carcinogenic to the respiratory system in sensitive inhalation bioassays. Although the exact mechanism is unknown, induction of tumours by these aldehydes is considered to be a function of both regenerative proliferative response and DNA–protein cross-linking at the site of contact.

Similarly, it has been proposed that the genotoxicity of acetaldehyde is based principally upon its ability to interact with single-stranded DNA during cell division (Feron *et al.*, 1982, 1984; Woutersen *et al.*, 1986; Roe and Wood, 1992; DECOS, 1993). Thus, a crucial determinant in the carcinogenicity of acetaldehyde in the nasal passages may be the cytotoxicity of this substance at high concentrations (Feron *et al.*, 1982, 1984; Woutersen *et al.*, 1986; Roe and Wood, 1992); cytotoxic concentrations of acetaldehyde cause recurrent tissue damage (and the presence of single-stranded DNA) and possess significant initiating activity. Moreover, the increased cell turnover may strongly enhance the fixation of relevant DNA damage and subsequently increase the progression of pre-cancer (initiated) cells to cancer.

However, the limited available data indicate that the pattern of DNA–protein cross-linking and proliferative response induced by acetaldehyde varies from that of other aldehydes, such as formaldehyde. For acetaldehyde, at concentrations at which tumours are observed (750 ppm [1350 mg/m^3]), there are increases in DNA–protein cross-links in the respiratory and olfactory mucosa of rats but no increase in proliferation (Cassee *et al.*, 1996a).[1] For formaldehyde, at the lower concentrations at which tumours are observed (6 ppm [7.2 mg/m^3]), there are increases in DNA–protein cross-links and proliferation in the nasal respiratory (but not olfactory) epithelium (Casanova *et al.*, 1994).

While acetaldehyde is genotoxic *in vitro* and *in vivo*, information concerning the potential roles of cytotoxicity, cell proliferation and DNA–protein cross-links in tumour formation is lacking.

2.4.4 Humans

Acetaldehyde is an upper respiratory tract and eye irritant in humans. The threshold concentration for the perception of acetaldehyde vapour may be as low as 0.2 µg/m^3 (Ruth, 1986). Ocular irritation has been observed at concentrations as low as 25 ppm (45 mg/m^3) acetaldehyde (Silverman *et al.*, 1946), while nasal and/or throat (sensory) irritation has been observed following exposure to concentrations just less than 200 ppm (360 mg/m^3) (Sim and Pattle, 1957).

Effects including headache, narcosis, decelerated heart rate and respiration, irritation of the eyes, skin, respiratory tract and throat, bronchitis, pulmonary edema, paralysis and death have been observed in individuals accidentally exposed to elevated levels of acetaldehyde (U.S. NRC, 1981a; ACGIH, 1991).

In patch tests, dermal irritation (i.e., cutaneous erythema) was observed in 12/12 volunteers exposed to a 75% aqueous solution of acetaldehyde (Wilkin and Fortner, 1985).

The only identified epidemiological study (Bittersohl, 1975) is considered inadequate to assess the carcinogenicity of acetaldehyde in humans, since it entailed only rather qualitative observations; there was no quantitative analysis by tumour site with a comparison population, standardizing for age and sex. Moreover, workers were exposed concomitantly to several other compounds.

[1] No increase in cell proliferation was observed in the nasal olfactory or respiratory epithelia of Wistar rats following repeated exposure (by inhalation) to concentrations up to 1500 ppm (2700 mg/m^3) acetaldehyde (concentrations similar to those that induced tumours in carcinogenesis bioassays in this strain) (Cassee *et al.*, 1996a).

3.0 ASSESSMENT OF "TOXIC" UNDER CEPA 1999

3.1 CEPA 1999 64(a): Environment

The environmental risk assessment of a PSL substance is based on the procedures outlined in Environment Canada (1997a). Analysis of exposure pathways and subsequent identification of sensitive receptors are the basis for selection of environmental assessment endpoints (e.g., adverse reproductive effects on sensitive fish species in a community). For each endpoint, a conservative Estimated Exposure Value (EEV) is selected and an Estimated No-Effects Value (ENEV) is determined by dividing a Critical Toxicity Value (CTV) by an application factor. A hyperconservative or conservative quotient (EEV/ENEV) is calculated for each of the assessment endpoints in order to determine whether there is potential ecological risk in Canada. If these quotients are less than one, it can be concluded that the substance poses no significant risk to the environment, and the risk assessment is completed. If, however, the quotient is greater than one for a particular assessment endpoint, then the risk assessment for that endpoint proceeds to an analysis where more realistic assumptions are used and the probability and magnitude of effects are considered. This latter approach involves a more thorough consideration of sources of variability and uncertainty in the risk analysis.

3.1.1 Assessment endpoints

Acetaldehyde enters the Canadian environment mainly from natural and anthropogenic combustion sources, notably vehicle emissions, from industrial on-site releases and through secondary formation as a result of the oxidation of anthropogenic and natural organic compounds in air. Almost all environmental formation and releases of acetaldehyde are to air, with small amounts released to water.

Given its physical-chemical properties, acetaldehyde undergoes various degradation processes in air, with very small amounts transferring into water. When released to water or soil, acetaldehyde is expected to remain primarily in the original compartment to which it was released, where it undergoes various biological and physical degradation processes. Acetaldehyde is not bioaccumulative or persistent in any compartment of the environment.

Based on the sources and fate of acetaldehyde in the ambient environment, biota are expected to be exposed to acetaldehyde primarily in air and, to a lesser extent, in water. Little exposure of soil or benthic organisms is expected. While acetaldehyde occurs naturally in plants and animals, it is readily metabolized and does not bioaccumulate in organisms. Therefore, the focus of the environmental risk characterization will be on terrestrial and aquatic organisms exposed directly to ambient acetaldehyde in air and water.

3.1.1.1 Terrestrial

Data on terrestrial toxicity are available for a variety of bacteria, fungi, plants and invertebrates (Section 2.4.1.1), as well as from mammalian toxicology studies (Section 2.4.3). Identified sensitive endpoints include the inhibition of growth of fungi (Yuen *et al.*, 1995), necrosis of plant leaves (Stewart *et al.*, 1980), mortality of insects (Aharoni *et al.*, 1979) and histopathological changes in nasal olfactory epithelium in rats (Appelman *et al.*, 1986).

Fungi are ubiquitous in terrestrial ecosystems and, as saprophytes, are essential for nutrient cycling. Terrestrial plants are primary producers, provide food and cover for animals and provide soil cover to reduce erosion and moisture loss. Invertebrates are an important component of the terrestrial ecosystem, both consuming plant

and animal matter and serving as forage for other animals. Vertebrate wildlife species are key consumers in most terrestrial ecosystems.

Therefore, although limited, the available toxicity studies cover an array of organisms from different taxa and ecological niches and are considered adequate for an assessment of risks to terrestrial biota. The single most sensitive response for all of these endpoints will be used as the CTV for the risk characterization for terrestrial effects.

3.1.1.2 Aquatic

Data on aquatic toxicity are available for a variety of microorganisms, algae, invertebrates and fish (Section 2.4.1.2). Identified sensitive endpoints include population growth of protozoans (Von Burg and Stout, 1991), the reduction of growth of algae (Stratton, 1987), immobilization of crustaceans (Von Burg and Stout, 1991) and mortality in fish (Brooke *et al.*, 1984).

Algae are primary producers in aquatic systems, forming the base of the aquatic food chain, while zooplankton, including protozoans and crustaceans, are key consumers and are themselves consumed by many species of invertebrates and vertebrates. Fish are consumers in aquatic communities and are themselves eaten by piscivorous fish, birds and mammals.

Therefore, although limited, the available studies cover an array of organisms from different taxa and ecological niches and are considered adequate for an assessment of risks to aquatic biota. The single most sensitive response for all of these endpoints is considered as the CTV for the risk characterization for aquatic effects.

3.1.2 Environmental risk characterization

3.1.2.1 Terrestrial organisms

Environmental exposure to acetaldehyde in air is expected to be greatest near sites of continuous release or formation of acetaldehyde, namely in urban centres and near industrial facilities releasing acetaldehyde. Extensive recent data for concentrations in air are available for urban, suburban and rural sites in Canada, and data covering a full year are available for the single largest industrial emitter of acetaldehyde.

The highest reported concentration of acetaldehyde in air in Canada is a monthly average concentration of 1150 $\mu g/m^3$, obtained at one sampling station at an industrial site in July 1996 (Environment Canada, 1997c). The overall mean concentration for all stations at the industrial site was 199 $\mu g/m^3$ over the year, with a median of 94 $\mu g/m^3$. By comparison, the single highest 24-hour concentration for urban air was 16.5 $\mu g/m^3$, while the highest one-month to one-year mean in a city was 3.35 $\mu g/m^3$ (Dann, 1998). The concentration of 1150 $\mu g/m^3$ will be used as the EEV in the hyperconservative analysis for terrestrial organisms.

For the exposure of terrestrial organisms to acetaldehyde in air, the CTV is 540 mg/m^3, based on a five-day exposure concentration causing a 95% reduction in fruit decay by the fungus *Penicillium italicum* (Yuen *et al.*, 1995). This LOEL was the most sensitive effect value retained from a moderate data set composed of acute and chronic toxicity studies conducted on at least 18 species of terrestrial bacteria, fungi, plants, invertebrates and mammals. While a slightly lower LOEL of 437 mg/m^3 was identified for histopathological changes in the nasal epithelium of rats (see Section 2.4.3.3.1), the studies retained for the dose–response analyses for inhalation by mammals had a slightly higher LOEL of 720 mg/m^3 (see Section 3.3.3.1 and Table 3).

The five-day exposure for *Penicillium* can be considered as chronic exposure (covering a significant portion of the life span of the organism). However, CTVs are preferably identified for lower levels of effects, and an application factor can account for the high level of effect (95% reduction in fruit decay) associated with the LOEL in this study. Thus, for the hyperconservative analysis, the ENEV for

terrestrial organisms is derived by dividing the CTV by a factor of 100. This factor accounts for the high level of effect associated with the LOEL and uncertainty surrounding the conversion of the chronic LOEL to a chronic no-effect value, the extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity. As a result, the ENEV is 5.4 mg/m^3 (5400 µg/m^3).

The hyperconservative quotient is calculated by dividing the EEV of 1150 µg/m^3 by the ENEV for *P. italicum*, as follows:

$$\text{Quotient} = \frac{\text{EEV}}{\text{ENEV}}$$

$$= \frac{1150\ \mu g/m^3}{5400\ \mu g/m^3}$$

$$= 0.21$$

Since the hyperconservative quotient is less than one, it is unlikely that acetaldehyde causes adverse effects on populations of terrestrial organisms in Canada.

3.1.2.2 Aquatic organisms

Environmental exposure to acetaldehyde in water is expected to be greatest near areas of high atmospheric concentrations (where some acetaldehyde can partition from air into water) and near spills or other potential point sources. Data for ambient surface water are available only for limited sampling at four drinking water treatment plants in urban areas in Ontario and Alberta and for groundwater at the site of the largest industrial emitter.

The highest concentration of acetaldehyde reported in surface water is 114 µg/L, obtained for a sample collected from the Detroit River near the Windsor pilot plant in December 1993 (Anderson *et al.*, 1994). While no data are available for concentrations in surface water near point sources, acetaldehyde was measured in groundwater at concentrations greater than the detection limit at four of 13 sampling stations at the industrial site; the highest concentration was 1300 µg/L (Environment Canada, 1997c). This value will be used as the EEV in the hyperconservative analysis for aquatic organisms, based on the conservative assumption that the groundwater could recharge directly to surface water at its full concentration.

For exposure of aquatic biota to acetaldehyde in water, the CTV is 30.8 mg/L, based on a 96-hour LC_{50} for the fathead minnow (Brooke *et al.*, 1984). This was the most sensitive value identified from a moderate data set composed of acute toxicity studies conducted on at least 12 species of aquatic microorganisms, algae, invertebrates and fish.

For a hyperconservative analysis, the ENEV is derived by dividing this CTV by a factor of 100. This factor accounts for the uncertainty surrounding the extrapolation from an acute LC_{50} to a chronic no-effects value, the extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity. The resulting ENEV is 0.308 mg/L (308 µg/L).

The hyperconservative quotient is calculated by dividing the EEV of 1300 µg/L by the ENEV, as follows:

$$\text{Quotient} = \frac{\text{EEV}}{\text{ENEV}}$$

$$= \frac{1300\ \mu g/L}{308\ \mu g/L}$$

$$= 4.22$$

Since the hyperconservative quotient is more than one, it is necessary to consider further the likelihood of biota being exposed to such concentrations in Canada.

It is highly unlikely that the groundwater at a single sampling station would recharge directly to surface water. A more realistic

representation of groundwater quality at the industrial site could be achieved using the median or mean concentration in groundwater at the 13 sampling stations. The median would be <50 µg/L (detection limit), while the mean could be calculated as being between 232 µg/L and 266 µg/L (assigning values of 0 µg/L or 50 µg/L, respectively, to samples reported as being below the detection limit). The highest of these values is 266 µg/L and can be used as a conservative estimate of possible concentrations in the event of surface recharge.

The conservative quotient is calculated by dividing the EEV of 266 µg/L by the ENEV, as follows:

$$\text{Quotient} = \frac{\text{EEV}}{\text{ENEV}}$$

$$= \frac{266\ \mu g/L}{308\ \mu g/L}$$

$$= 0.86$$

Alternatively, a conservative quotient can be calculated using the single highest concentration measured in ambient water (114 µg/L obtained from the Detroit River). The conservative quotient calculated by dividing the EEV of 114 µg/L by the ENEV is:

$$\text{Quotient} = \frac{\text{EEV}}{\text{ENEV}}$$

$$= \frac{114\ \mu g/L}{308\ \mu g/L}$$

$$= 0.37$$

Since these two conservative quotients are less than one, it is unlikely that acetaldehyde causes chronic adverse effects on populations of aquatic organisms in Canada.

A summary of the critical values for the environmental risk analysis of acetaldehyde is presented in Table 2.

3.1.2.3 Discussion of uncertainty

There are a number of potential sources of uncertainty in this environmental risk assessment. Regarding effects of acetaldehyde on terrestrial and aquatic organisms, there is uncertainty concerning the extrapolation from available toxicity data to potential ecosystem effects. While the toxicity data set included studies on organisms from a variety of ecological niches and taxa, there are relatively few good chronic studies available. To account for these uncertainties, application factors were used in the environmental risk analysis to derive ENEVs.

Regarding environmental exposure, there could be concentrations of acetaldehyde in Canada that are higher than those identified and used in this assessment.

Few data are available for concentrations of acetaldehyde in air near point sources. However, the measurements used in this assessment are considered acceptable because they were selected from an extensive set of recent air monitoring data of urban and other sites and from data at the industrial facility with the highest reported import, production, use and release of acetaldehyde in Canada. These sites can also be associated with high concentrations of volatile organic compounds associated with secondary formation of acetaldehyde. Thus, available data on atmospheric concentrations are considered representative of the highest concentrations likely to be encountered in air in Canada.

Only limited data are available for concentrations of acetaldehyde in water, although concentrations are expected to be low because of the limited releases to this medium that have been identified and the limited partitioning of acetaldehyde from air into water. The available data on concentrations in groundwater are from the site of the largest emitter of acetaldehyde, and it can reasonably be expected that concentrations are the highest likely to occur in Canada. Since data are not available regarding surface recharge of the contaminated groundwater, the assessment

TABLE 2 Summary of the hyperconservative and conservative environmental risk analysis

Exposure scenario	EEV	CTV	Application factor	ENEV	Quotient (EEV/ENEV)
Terrestrial organisms: highest concentration in air at industrial site	1150 µg/m³	540 000 µg/m³	100	5400 µg/m³	0.21
Aquatic organisms: highest concentration in groundwater at industrial site	1300 µg/L	30 800 µg/L	100	308 µg/L	4.22
Aquatic organisms: mean concentration in groundwater at industrial site	266 µg/L	30 800 µg/L	100	308 µg/L	0.86
Aquatic organisms: highest concentration in surface water	114 µg/L	30 800 µg/L	100	308 µg/L	0.37

very conservatively assumed that recharge occurred at concentrations equivalent to those measured in the groundwater.

Despite some data gaps regarding the environmental effects and exposure of acetaldehyde, the data available at this time are considered adequate for making a conclusion on the environmental risk of acetaldehyde in Canada.

3.2 CEPA 1999 64(b): Environment upon which life depends

Acetaldehyde does not deplete stratospheric ozone and its potential for climate change is negligible. The photolysis of acetaldehyde leads to the direct formation of radicals that are active in the formation of ground-level ozone (Carter *et al.*, 1995). It is more reactive (POCP of 121) than compounds such as ethene that are recognized as important in the formation of ground-level ozone. Given its reactivity and concentrations measured in air in Canada, acetaldehyde represented approximately 3.4% of the total volatile organic carbon reactivity, ranking it 8th among non-methane hydrocarbons and carbonyl compounds contributing to the formation of ground-level ozone (Dann and Summers, 1997). Acetaldehyde, along with other reactive volatile organic chemicals, may therefore be important in the photochemical formation of ground-level ozone in urban areas. It is therefore concluded that acetaldehyde is considered "toxic" as defined in CEPA Paragraph 64(b).

3.3 CEPA 1999 64(c): Human health

3.3.1 Estimated population exposure

Point estimates of total daily intakes of acetaldehyde by six age groups of the general population of Canada were developed primarily to determine the relative contributions from various media. These estimates indicate that the daily intake of acetaldehyde via inhalation is consistently less than that by ingestion, although it should be noted that no data on concentrations of acetaldehyde in foodstuffs in Canada were identified. Also, though intermediary metabolism and ingestion of alcoholic beverages contribute to levels of acetaldehyde in the body, critical effects of exposure to exogenous acetaldehyde, based on studies in animals, occur at the site of first contact

(i.e., the respiratory tract following inhalation and the gastrointestinal tract following ingestion). For this reason, effects of exposure by different routes are addressed separately. However, available toxicological data are inadequate to serve as a basis for development of a measure of dose–response for critical site of contact effects following ingestion. Probabilistic estimates of 24-hour time-weighted concentrations of acetaldehyde in the air to which Canadians are exposed have been developed, therefore, for comparison with the Tolerable Concentration (TC) in this medium. This approach is also supported on the basis that anthropogenic emissions of acetaldehyde are released principally to air, where it degrades, with little movement into other media.

In this exposure scenario, the general population is considered to be exposed to acetaldehyde in air for a full 24 hours per day. The exposure is assumed to occur by inhalation of ambient (outdoor) air and indoor air. When indoors, it is assumed that the general population is exposed to acetaldehyde concentrations similar to those in the indoor air of their homes, as there are insufficient data concerning concentrations in other indoor environments.

This exposure scenario requires consideration of the proportion of the 24-hour day that is spent indoors versus the proportion spent outdoors. A mean time spent outdoors of three hours is assumed based on point estimates of time spent indoors and outdoors (Environmental Health Directorate, 1997). The distribution of the time spent outdoors is arbitrarily assumed to be normal in shape with an arithmetic standard deviation of one hour. The time spent indoors is calculated as 24 hours minus the time spent outdoors.

To represent the concentrations of acetaldehyde in ambient air, the distribution of the 24-hour concentrations from the National Air Pollution Surveillance (NAPS) Program (Dann, 1998) was selected, in which individual data were available for 2805 samples of ambient air collected (between 1989 and 1997) at 14 rural, urban and suburban locations in six provinces (New Brunswick, Nova Scotia, Quebec, Ontario, Manitoba and British Columbia). Acetaldehyde was detected in 99.8% of samples (detection limit 0.1 $\mu g/m^3$) in this data set.

For concentrations of acetaldehyde in indoor air, the (limited) results of the only identified relevant investigation in Canada, the Windsor Air Quality Study (Bell *et al.*, 1993; OMEE, 1994a,b; Bell, 1995, 1996, 1997), were selected. The concentrations of acetaldehyde in 47 samples of indoor air from homes in Windsor and Hamilton, Ontario, were measured between 1991 and 1993. Acetaldehyde was detected in all of the samples (detection limit 0.1 $\mu g/m^3$) in this data set.

Estimates of the distribution of time-weighted 24-hour concentrations of acetaldehyde to which the general population is exposed were developed using simple random sampling with Crystal Ball™ Version 4.0 (Decisioneering, Inc., 1996) and simulations of 10 000 trials. This process was repeated for a total of five simulations to assess the reproducibility of the estimates.

Based on the assumptions underlying this scenario, one person in every two would be exposed to a 24-hour average concentration of acetaldehyde of 14 $\mu g/m^3$ (i.e., median concentration) or greater, and one in 20 persons (i.e., 95th percentile) would be exposed to a 24-hour average concentration of at least 52 μg acetaldehyde/m^3.

In addition, as described in Section 2.3.2.1, there are data on concentrations of acetaldehyde in the vicinity of industrial sources in Canada. While there is no indication of the proximity of monitoring sites to residential areas, the average monthly concentrations at four monitoring stations at a chemical plant in Edmonton, Alberta, considered to be the largest emitter in Canada throughout 1996, ranged from below the detection limit of 1.8 $\mu g/m^3$ at some stations up to a maximum of 1150 $\mu g/m^3$ at one station in July. The overall mean concentration

for all stations was 199 µg/m³, with a median of 94 µg/m³ (Environment Canada, 1996a, 1997b,c).

3.3.2 Hazard characterization

3.3.2.1 Effects in humans

Data relevant to the assessment of the potential adverse effects of exposure to acetaldehyde in humans are limited primarily to irritation. Based on early clinical studies of small numbers of volunteers exposed for short periods, ocular and nasal/throat irritation have been observed at concentrations as low as 25 ppm (45 mg/m³) and just less than 200 ppm (360 mg/m³), respectively (Silverman *et al.*, 1946; Sim and Pattle, 1957). The only identified epidemiological study (Bittersolh, 1975) is inadequate to serve as a basis for assessment of the carcinogenicity of acetaldehyde.

Due to the limited nature of the human data, hazard characterization and dose–response analysis for acetaldehyde are based primarily on studies in animals.

3.3.2.2 Effects in experimental animals

Acetaldehyde has low acute toxicity, is irritating to the skin, eyes and upper respiratory tract, and induces sensory irritation in rodents.

The effects of acetaldehyde have been most extensively investigated following exposure by inhalation. In short- and long-term inhalation studies in rats and hamsters, the target tissue has consistently been the site of entry, with non-neoplastic and neoplastic effects occurring principally in the upper respiratory tract at lowest concentrations, without appreciable effects in other organ systems. (Systemic effects in repeated-exposure studies, generally observed at concentrations considerably higher than the lowest concentrations that induce effects in the respiratory tract, have been confined to effects on body and some organ weights, hematological parameters and some liver enzymes.) This is consistent with observations in toxicokinetic studies in rats and humans, in which the highest proportion of inhaled acetaldehyde is retained at the site of contact.

In repeated-exposure inhalation studies, species-related differences in sensitivity to acetaldehyde have been observed. Available data indicate that hamsters are less sensitive than rats, with adverse effects in the respiratory tract appearing at higher vapour concentrations. Moreover, inhalation of acetaldehyde in hamsters results in lesions in more distal airways (i.e., larynx, trachea), whereas effects in rats at the lowest exposure concentrations are confined primarily to the proximal airways (i.e., nasal cavity). At lowest concentrations, degenerative changes have been observed in the olfactory epithelium in rats and the trachea in hamsters. At higher concentrations, degenerative changes in the respiratory epithelium and larynx have been noted in both species. The proximal to distal pattern of lesions with increasing concentration observed in the inhalation studies is consistent with the reactivity and solubility of acetaldehyde.

In long-term inhalation studies, an increased incidence of tumours has been observed in rats and hamsters at concentrations that induce damage in the respiratory tract. In rats, there were concentration-related increases in adenocarcinomas of the olfactory epithelium and squamous cell carcinomas of the respiratory epithelium, with the latter being predominant and occurring at lowest concentrations (Woutersen *et al.*, 1986). In hamsters, significant increases in laryngeal carcinomas and non-significant increases in nasal carcinomas (site not specified) have been reported (Feron *et al.*, 1982).

Data for ingestion are limited to one short-term study conducted in rats in which a wide range of endpoints was examined (Til *et al.*, 1988) and one subchronic investigation in which only overt toxicity, body weight gain and hepatic effects were examined in rats (Matysiak-Budnik *et al.*, 1996), both following ingestion in drinking water. Consistent with observations for inhalation, effects were observed at the portal of entry, with

hyperkeratosis of the forestomach observed in rats (Til *et al.*, 1988).

Available data are inadequate to serve as a basis for assessment of the carcinogenicity of acetaldehyde following ingestion. Tumours were not observed in the only long-term ingestion study identified (Matysiak-Budnik *et al.*, 1996). However, this investigation was limited by small group sizes and the very limited range of endpoints examined (i.e., only histopathology in the liver examined).

Available data are inadequate to assess the potential reproductive, developmental, neurological or immunological effects of direct exposure to acetaldehyde. Based on the limited number of investigations conducted to date, however, reproductive, developmental, neurological and immunological effects have not been observed at concentrations below those that induce damage in the upper respiratory tract (Ortiz *et al.*, 1974; Kruysse *et al.*, 1975; Shiohara *et al.*, 1985; Aranyi *et al.*, 1986; Roumec *et al.*, 1988).

Acetaldehyde has induced a broad spectrum of mutagenic, clastogenic and aneugenic effects *in vitro*. Although the number of relevant studies is limited, there is also evidence that acetaldehyde is genotoxic *in vivo*.

3.3.3 Dose–response analyses

3.3.3.1 Inhalation

In inhalation studies conducted in rodents, the respiratory tract has consistently been affected at lowest concentrations, with similar effects noted in the critical studies, although with some species variation in sensitivity and principal site. In identified short-term investigations, degenerative changes (including inflammation, hyperplasia, thinning and disarrangement of epithelial cells, and loss of microvilli and sensory cells) and associated functional effects were observed in the nasal olfactory epithelium in rats exposed (by inhalation) to ≥243 ppm (≥437 mg/m^3) acetaldehyde, while degenerative changes in the nasal respiratory epithelium, larynx, trachea and lungs were observed at higher concentrations (i.e., ≥1000 ppm [≥1800 mg/m^3]) (Appelman *et al.*, 1982, 1986; Saldiva *et al.*, 1985; Cassee *et al.*, 1996a). In the only subchronic inhalation study identified, in which hamsters were exposed to acetaldehyde for 13 weeks (Kruysse *et al.*, 1975), non-neoplastic lesions in the tracheal epithelium (including stratification, keratinization, inflammation, metaplasia and granulation) were observed at ≥1340 ppm (≥2412 mg/m^3) acetaldehyde (considered to be the LOAEL), while histopathological lesions in the nasal cavities, larynx, bronchi and lungs were observed only at 4560 ppm (8208 mg/m^3) acetaldehyde; the NOEL in this study was considered to be 390 ppm (702 mg/m^3) acetaldehyde (Kruysse *et al.*, 1975). In chronic inhalation studies in which rats were exposed to acetaldehyde for up to 28 months, focal basal cell hyperplasia of the nasal olfactory epithelium was observed at ≥750 ppm (≥1350 mg/m^3) acetaldehyde (considered to be the LOAEL), while non-neoplastic lesions in the nasal respiratory epithelium (squamous metaplasia, papillomatous hyperplasia, and focal or pseudoepitheliomatous hyperplasia) and larynx (squamous metaplasia and hyperplasia) were observed at concentrations ≥1500 ppm (≥2700 mg/m^3) acetaldehyde (Woutersen *et al.*, 1984, 1986; Feron *et al.*, 1985; Woutersen and Feron, 1987). Similarly, non-neoplastic lesions in the nasal epithelia, larynx and trachea have been observed in hamsters exposed by inhalation to ≥1500 ppm (≥2700 mg/m^3) acetaldehyde for 52 weeks (Feron, 1979; Feron *et al.*, 1982).

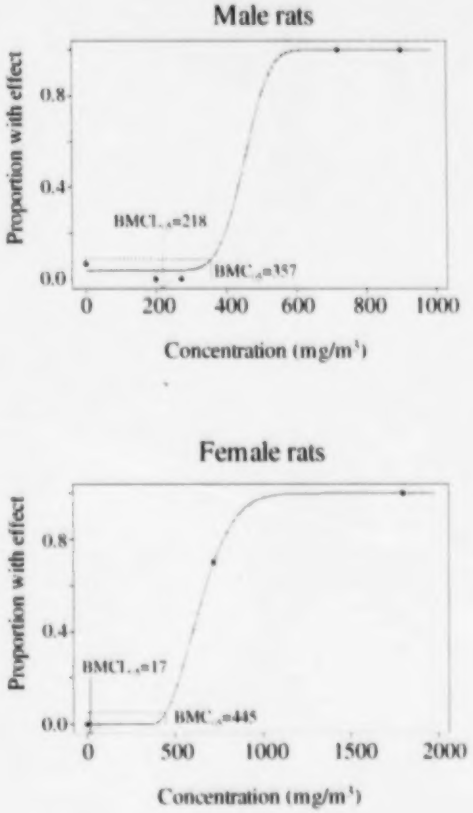
A tolerable concentration (TC) for acetaldehyde has been derived on the basis of a benchmark concentration (BMC) for non-neoplastic effects in the respiratory tract of rats, the most sensitive species, divided by an uncertainty factor. This BMC is compared with Tumorigenic Concentrations (TC_{05}s, the concentrations associated with a 5% increase in the incidence of relevant tumours) in rats. Despite differences in the anatomy and physiology of the respiratory tract in rats and humans, respiratory tract defence mechanisms are similar. Thus, it is reasonable to assume that the response of the human respiratory

tract mucosa to acetaldehyde will be qua'.tatively similar to that of experimental species, although the likely site of development of lesions may vary due to oro-nasal breathing patterns in humans, which result in greater potential to deliver acetaldehyde to the lower respiratory tract.

The studies that provide best characterization of concentration–response for the critical effects in the most sensitive species (i.e., rats) are the short-term studies of Appelman *et al.* (1982, 1986). Therefore, a TC has been developed on the basis of BMCs for degeneration in the nasal olfactory epithelium of Wistar rats exposed to acetaldehyde (by inhalation) for four weeks, using combined data from the critical studies for characterization of concentration–response mentioned above (Appelman *et al.*, 1982, 1986). The value is also compared with that which might be derived based on the NOEL in rats (Appelman *et al.*, 1986).

For many types of effects, studies of short duration are not preferred as the basis for development of a TC. Although the data were derived from short-term studies, the incidence of degenerative changes in the olfactory epithelium was not dissimilar to that observed in the same strain of rats in the long-term carcinogenesis bioassay at similar concentrations, conducted by Woutersen *et al.* (1986). Although group sizes were larger in the long-term bioassay, concentration–response for these lesions was not well characterized because of the small number of dose groups exposed to higher concentrations compared with the short-term study and early mortality among animals at the highest concentration. Indeed, data in the Woutersen *et al.* (1986) study are insufficient to serve as a basis for development of a meaningful BMC for acetaldehyde, even simply for purposes of comparison. Therefore, BMCs for non-neoplastic effects have been calculated for degeneration in the nasal olfactory epithelium of Wistar rats exposed (by inhalation) to acetaldehyde for four weeks, based on data from the critical studies by Appelman *et al.* (1982, 1986). The critical data are presented in Table 3. Using the THRESH program (Howe, 1995), the BMC_{05} (the concentration associated with a 5% increase in the incidence of nasal olfactory epithelial lesions) for male Wistar rats is 357 mg/m^3; the lower 95% confidence limit for this value ($BMCL_{05}$) is 218 mg/m^3. For female Wistar rats, the BMC_{05} and $BMCL_{05}$ are 445 mg/m^3 and 17 mg/m^3,

FIGURE 1 $BMCL_{05}$s for effects in the nasal olfactory epithelium (without correction for continuous exposure)



respectively (Figure 1). A TC has been developed on the basis of the $BMCL_{05}$ for non-neoplastic lesions in the nasal olfactory epithelium of rats as follows:

$$TC = \frac{218\ mg/m^3}{100} \times \frac{6}{24} \times \frac{5}{7}$$

$$= 390\ \mu g/m^3$$

TABLE 3 Benchmark concentrations (BMC_{05}s and $BMCL_{05}$s) for acetaldehyde based on the incidence of degenerative changes in the nasal olfactory epithelium of Wistar rats (Appelman *et al.*, 1982, 1986)

Concentration, mg/m³ (ppm)	Incidence of degenerative changes	Benchmark concentration (without adjustment for continuous exposure)	Parameter estimates
Males			
0	2/30		
198 (110)	0/10	5% concentration: 357 mg/m³	Chi-square goodness of fit: 1.3×10^{-8}
270 (150)	0/10		
720 (400)	9/10	95% confidence limit: 218 mg/m³	Degrees of freedom: 0
900 (500)	10/10		
1800 (1000)	10/10		p-value: 1.00
3960 (2200)	9/9		
9000 (5000)	10/10		
Females			
0	0/10		
198 (110)	NA[1]	5% concentration: 445 mg/m³	Chi-square goodness of fit: 1.3×10^{-8}
270 (150)	NA		
720 (400)	7/10	95% confidence limit: 17 mg/m³	Degrees of freedom: 0
900 (500)	NA		
1800 (1000)	10/10		p-value: 1.00
3960 (2200)	10/10		
9000 (5000)	10/10		

[1] NA = not available.

where:

- 218 mg/m³ is the 95% lower confidence limit of the concentration estimated to be associated with a 5% increase in non-neoplastic lesions in the nasal olfactory epithelium of male Wistar rats (the most sensitive sex and that for which the data set is most robust) exposed by inhalation to acetaldehyde for four weeks (Appelman *et al.*, 1982, 1986);
- 6/24 and 5/7 are the adjustments of intermittent (six hours per day for five days per week) to continuous exposure. There are no data that provide direct evidence and few related data to serve as a basis for whether or not such an adjustment is appropriate for acetaldehyde. In short-term studies in the same strain of rats, effects seemed slightly more severe following exposure for eight hours per day (Saldiva *et al.*, 1985) versus six hours per day for four weeks (Appelman *et al.*, 1986). Interruption of daily exposure by 1.5-hour exposure-free periods or by the superimposition of eight five-minute peak exposure periods did not appreciably influence the cytotoxic potency of acetaldehyde in short-term studies in rats compared with uninterrupted exposure to a fixed concentration (Appelman *et al.*, 1986); and,
- 100 is the uncertainty factor (×10 for interspecies variation, ×10 for intraspecies variation). Available data are inadequate to further address toxicokinetic and toxicodynamic aspects of components of uncertainty with data-derived values.

The value for interspecies variation is considered to be conservative since, due to greater penetration of inhaled gases into the lower airways of rodents versus humans, the compound is distributed over a larger surface area for the latter; available data are inadequate, however, to quantitatively account for this variation. No additional quantitative element has been included to address limitations of the database such as lack of adequate developmental or reproductive studies by a relevant route of exposure, due to the fact that a TC that is based on critical effects at the site of entry is likely to be protective for systemic effects. Also, in view of the fact that there is no indication that severity of the critical effects increases with duration of exposure, an additional quantitative element to address the use of a shorter-term study as the basis for the TC is considered inappropriate.

This TC is similar to that derived from the NOEL for irritation in the most sensitive species (Wistar rats), identified in the short-term study of Appelman *et al.* (1986). Based on the NOEL of 270 mg/m^3 (150 ppm), with adjustment for intermittent to continuous exposure (6/24 × 5/7) and an uncertainty factor of 100 (×10 for interspecies variation, ×10 for intraspecies variation), the resulting value is 490 µg/m^3.

On the basis of limited available data in human studies, the TCs derived above (390 and 490 µg/m^3) are two orders of magnitude lower than the threshold for sensory irritation (i.e., 45 mg/m^3 [25 ppm]) (Silverman *et al.*, 1946).

In view of the genotoxicity of acetaldehyde and relative lack of information concerning the mechanism of induction of tumours for this substance, an estimate of the carcinogenic potency (TC_{05}) has also been derived, based on the increased incidence of nasal tumours (squamous cell carcinoma, adenocarcinoma and carcinoma *in situ*) in male and female Wistar rats exposed (by inhalation) to acetaldehyde for up to 28 months (Woutersen *et al.*, 1986). This was the only study in which carcinogenicity was investigated in the most sensitive species (i.e., rats). It was also considered the most appropriate for quantitative assessment of the TC_{05} of acetaldehyde, owing to the larger size of the study group (n = 55 compared with 18–35 in hamsters), the longer duration of the exposure period (28 months versus 12 months in hamsters) and the larger number of exposure concentrations (three concentrations and controls).

The critical data upon which the TC_{05}s are based are presented in Table 4. The highest concentration group was not included in the derivation, since exposure levels were decreased gradually from 5400 to 1800 mg/m^3 due to high mortality. The TC_{05}s and lower 95% confidence limits (TCL_{05}s) (presented in Table 4, Figures 2 and 3) were calculated using a multistage model, with adjustment for intermittent to continuous exposure (6/24 × 5/7). Inclusion of an f^2 term to account for the fact that tumours occur more frequently later in life (where f is the length of the experiment divided by the standard lifetime) was unnecessary, since animals in the critical study were exposed for up to 28 months and killed at weeks 120–122. Values have not been adjusted by the ratio of inhalation to body weight, since tumours were restricted to the site of exposure. With adjustment for intermittent to continuous exposure, the resultant TC_{05} for nasal adenocarcinomas and squamous cell carcinomas in the most sensitive sex (males) is 86 mg/m^3, while the TCL_{05} is 28 mg/m^3. These values are approximately twofold higher than and the same as the TC_{05} and TCL_{05}, respectively, for adenocarcinomas alone and three- and sixfold less than the TC_{05} and TCL_{05}, respectively, for squamous cell carcinomas alone.

3.3.3.2 Ingestion

Available data are inadequate to provide quantitative guidance concerning the potential risks associated with ingestion of acetaldehyde. Data are limited to one short-term study in rats in which a wide range of endpoints was examined (Til *et al.*, 1988) and one subchronic investigation

TABLE 4 Tumorigenic concentrations (TC_{05}s and TCL_{05}s) for acetaldehyde based on the incidence of tumours in the nasal cavity of Wistar rats (Woutersen *et al.*, 1986)

Tumour type	Concentration, mg/m³ (ppm)[1]	Tumour incidence[2,3]	TC_{05} (TCL_{05}) (without correction for continuous exposure)	TC_{05} (TCL_{05}) (with correction for continuous exposure)[4]	Parameter estimates
Males					
Squamous cell carcinoma	0	1/49	1508 (906)	271 (163)	Chi-square = 1.62
	1350 (750)	1/52			Degrees of freedom = 1
	2700 (1500)	10/53*			p-value = 0.20
	5400/1800 (3000/1000)	15/49***			
Adenocarcinoma	0	0/49	225 (135)	41 (24)	Chi-square = 0.00
	1350 (750)	16/52***			Degrees of freedom = 1
	2700 (1500)	31/53***			p-value = 1.00
	5400/1800 (3000/1000)	21/49***			
Carcinoma *in situ*[5]	0	0/49	– (–)	– (–)	
	1350 (750)	0/52			
	2700 (1500)	0/53			
	5400/1800 (3000/1000)	1/49			
Combined	0	1/49	478 (157)	86 (28)	Chi-square = 0.00
	1350 (750)	17/52			Degrees of freedom = 0
	2700 (1500)	41/53			p-value = –
	5400/1800 (3000/1000)	–			
Females					
Squamous cell carcinoma	0	0/50	2161 (1374)	389 (247)	Chi-square = 1.20
	1350 (750)	0/48			Degrees of freedom = 2
	2700 (1500)	5/53			p-value = 0.55
	5400/1800 (3000/1000)	17/53***			
Adenocarcinoma	0	0/50	731 (365)	132 (66)	Chi-square = 0.58
	1350 (750)	6/48*			Degrees of freedom = 2
	2700 (1500)	28/53***			p-value = 0.75
	5400/1800 (3000/1000)	21/53***			
Carcinoma *in situ*	0	0/50	2813 (2700)	506 (486)	Chi-square = 0.70
	1350 (750)	0/48			Degrees of freedom = 2
	2700 (1500)	3/53			p-value = 0.70
	5400/1800 (3000/1000)	5/53			
Combined	0	0/50	621 (400)	112 (72)	Chi-square = 3.09
	1350 (750)	6/48			Degrees of freedom = 2
	2700 (1500)	36/53			p-value = 0.21
	5400/1800 (3000/1000)	–			

[1] The highest concentration was gradually reduced from 5400 mg/m³ during the first 20 weeks to 1800 mg/m³ in week 52; the time-weighted average concentration for 28 months of exposure was calculated by the Task Group to be 2760 mg/m³.

[2] Total number of tumour-bearing animals not specified.

[3] Significance: Fisher Exact Test, * $p < 0.05$, *** $p < 0.001$.

[4] The TC_{05}s were multiplied by (6 hours per day/24 hours per day) × (5 days per week/7 days per week) to adjust for intermittent to continuous exposure.

[5] The Tumorigenic Concentration for carcinoma *in situ* in male rats cannot be calculated since the highest concentration group was eliminated and all three remaining groups had zero response.

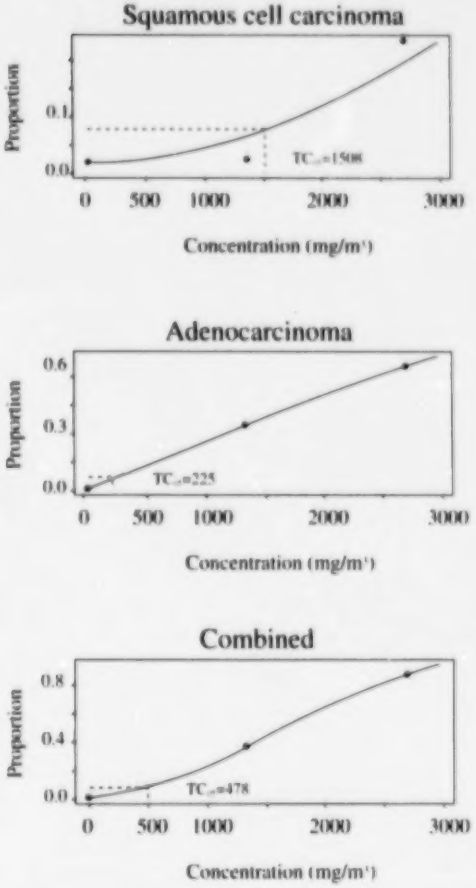
in which only a very limited range of endpoints was considered (Matysiak-Budnik *et al.*, 1996), both via ingestion in drinking water. In the latter study, non-neoplastic changes in the liver (microvesicular fatty degeneration, fatty accumulation and foci of inflammatory cells) were observed at 500 mg acetaldehyde/kg-bw per day (considered to be the LOAEL), while no effects were observed at 120 mg acetaldehyde/kg-bw per day (considered to be the NOEL). Effect levels were similar in the short-term study conducted in the same strain of rats, in which the LOAEL and NOEL were 675 and 125 mg acetaldehyde/kg-bw per day, respectively, based on focal hyperkeratosis of the forestomach and increased renal weight (Til *et al.*, 1988). Interestingly, results of the short-term study contrast somewhat with those of the longer-term study of Matysiak-Budnik *et al.* (1996), since hepatic effects were not observed at 675 mg/kg-bw per day in the former.

3.3.4 Human health risk characterization

While the cytotoxicity of acetaldehyde along with the induction of DNA–protein cross-links are likely crucial determinants in the carcinogenicity of this compound at high concentrations, there is a relative lack of information concerning their potential roles in tumour induction. Indeed, available data are inadequate to quantitatively take both of these likely endpoints into account in development of measures of dose–response relevant to the general population. Moreover, based on limited available data, the pattern of DNA–protein cross-linking, cytotoxicity and proliferative response induced by acetaldehyde varies from that of other aldehydes such as formaldehyde.

For compounds such as acetaldehyde, where data are insufficient to quantitatively adequately assimilate the information on likely intermediate endpoints in development of measures of dose–response, and in view of the genotoxicity of the compound both *in vitro* and *in vivo*, estimates of exposure are compared with quantitative estimates of cancer potency (Exposure Potency Index)

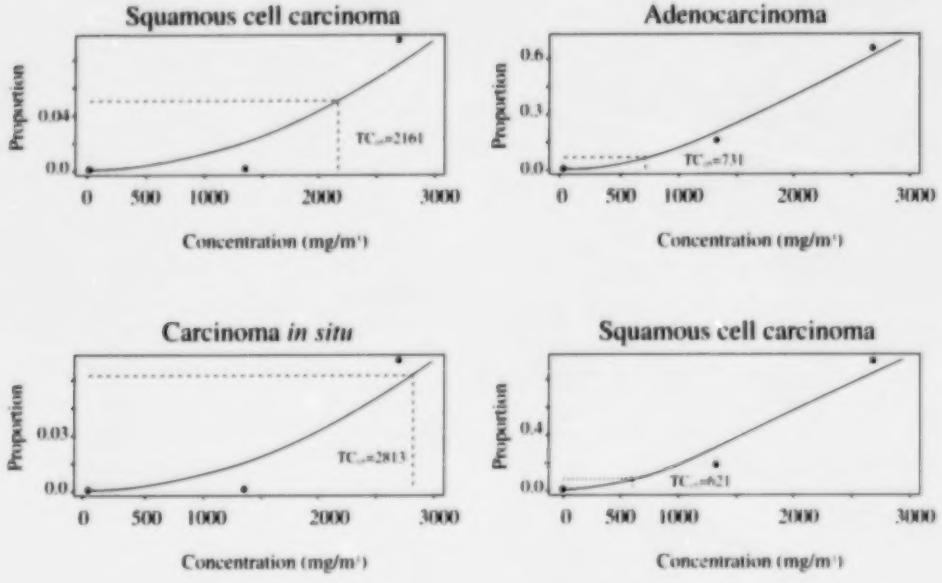
FIGURE 2 TC_{05}s for male Wistar rats (without correction for continuous exposure)



to characterize risk and provide guidance in establishing priorities for further action (i.e., analysis of options to reduce exposure) under CEPA.

However, in view of the likely critical role of cytotoxicity as well as genotoxicity in the carcinogenicity of this compound, measures of cancer potency are compared with those for non-cancer effects. Exposure of the general population is also compared with the TC for non-neoplastic effects.

FIGURE 3 TC_{05}s for female Wistar rats (without correction for continuous exposure)



The lowest TC_{05} was 86 mg/m³ for nasal adenocarcinomas and squamous cell carcinomas in the male rat; the lower 95% confidence limit was 28 mg/m³. Based upon probabilistic estimates of 24-hour time-weighted concentrations of acetaldehyde in air in Canada, median and and 95th percentiles are estimated to be 13.5 and 51.7 µg/m³, respectively. These estimated concentrations are three orders of magnitude less than the TC_{05} and TCL_{05}.[2] On this basis, priority for investigation of options to reduce exposure is considered moderate.

It is of some interest that the measure of carcinogenic potency (TC_{05} of 86 mg/m³) is similar to but slightly less than a comparable value for non-cancer effects (i.e., $BMCL_{05}$ of 218 mg/m³).

The median and 95th percentile estimates of the 24-hour time-weighted concentrations of acetaldehyde in air in Canada discussed above are one order of magnitude less than the TC for acetaldehyde for non-neoplastic effects.

While there is no indication of the proximity of monitoring sites to residential areas, average monthly concentrations at four monitoring stations at a chemical plant in Edmonton, Alberta, considered to be the largest emitter in Canada, are 1–4 orders of magnitude less than the TC_{05} and TCL_{05}. Based upon the median concentration of acetaldehyde (i.e., 94 µg/m³) determined at these monitoring stations, concentrations of acetaldehyde in ambient air near industrial point sources are three orders of magnitude less than the TC_{05} and TCL_{05}.[3] On this basis, priority for investigation of options to reduce exposure is considered to be high. In addition, these values approach and exceed the TC based on non-neoplastic effects.

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[2] For comparison with Exposure Potency Indexes for PSL 1 compounds where exposure was expressed as a proportion of potency, the relevant value is 1.5×10^{-4}.

[3] For comparison with Exposure Potency Indexes for PSL 1 compounds where exposure was expressed as a proportion of potency, the relevant value is 1.1×10^{-1}.

3.3.5 *Uncertainties and degree of confidence in human health risk characterization*

There are a number of uncertainties associated with the human health risk characterization of acetaldehyde.

Uncertainty associated with data on concentrations of acetaldehyde in outdoor air from the 14 NAPS sites is judged to be low, since the analytical and sampling methodologies are among the best available for determining low concentrations of acetaldehyde in air. Moreover, all of the samples were analysed by a single specialized laboratory, the effects of diurnal variations were minimized by the 24-hour sampling duration, the data set is large (n = 2805) and reasonably current (i.e., 1989 to early 1997), acetaldehyde was present in concentrations greater than the limit of detection (i.e., 0.1 mg/m^3) in a high proportion of the samples (i.e., >99%) and the concentrations of acetaldehyde measured are consistent with concentrations reported for outdoor air in other Canadian and international studies. However, some uncertainty is expected, since the locations of the 14 NAPS sites were not determined by a random sampling scheme, and, at some sites, the air is sampled at elevations higher than the breathing zone. The greatest source of uncertainty in the estimates of exposure in air is attributable to lack of information concerning geographical population distribution in relation to the NAPS monitoring sites. However, samples from Canada's three major urban centres (i.e., Montréal, Quebec; Toronto, Ontario; Vancouver, B.C.) account for 49% of the NAPS samples, and samples from three other cities (i.e., Saint John, New Brunswick; Ottawa, Ontario; Windsor, Ontario) account for another 39%.

Uncertainty associated with data on concentrations of acetaldehyde in indoor air from two studies in Canada was judged to be moderate. The analytical and sampling methodologies are among the best available for determining low concentrations of acetaldehyde in air, all of the samples were analysed by a single specialized laboratory, the sampling and analytical methodologies were the same as those employed for measuring the outdoor (ambient) concentrations in the NAPS data set, the effects of diurnal variations are minimized by the 24-hour sampling duration, the studies are reasonably current (i.e., 1991–1993), acetaldehyde was detected in all of the 47 samples, and the concentrations of acetaldehyde measured are consistent with limited data reported for residential indoor air in other studies, especially those that are more recent. However, some uncertainty is introduced because this is a very small data set, the homes sampled were not selected by a random sampling scheme and often involved volunteers, homes in Windsor and Hamilton may not be representative of all homes in Canada, and indoor locations other than home (e.g., work sites, public places, vehicle cabins) are not included. Additional uncertainty is introduced in the probabilistic assessment of intakes, since the actual distribution of concentrations in indoor air is represented by an assumed lognormal distribution; however, this is expected to make a minor contribution to the overall uncertainty associated with estimates of intake of acetaldehyde by the inhalation route.

Uncertainty concerning the time spent indoors by Canadians is judged to be low, since the estimate is based on the most current Canadian data, a random sampling scheme was used to obtain the time–activity data, and analysis of the data involved population weighting; however, the same mean time spent outdoors is assumed for Canadians of all age groups and in all regions of the country, a normal distribution is assumed for the hours per day spent outdoors, and the variance of the assumed normal distribution is also assumed (i.e., standard deviation of one).

There is a high degree of uncertainty concerning the content of acetaldehyde in food currently consumed by Canadians. Data on concentrations in this medium are restricted to a very small number of food samples collected in other countries, and details concerning the numbers of samples analysed and the locations and dates of sample acquisition are lacking. Based

on the known widespread natural occurrence of acetaldehyde in a variety of foods, estimates based on the limited reported data are likely less than the true intake. However, acetaldehyde is not expected to partition into the fatty compartments of foods, and fugacity modelling does not predict significant bioconcentration.

There is a moderate degree of certainty that consumption of drinking water does not contribute significantly to the daily intake of acetaldehyde by Canadians, based on sensitive measurements of Canadian water from a small number of treatment plants in Alberta and Ontario. However, these data are lacking in terms of numbers of samples collected and the frequency of detection of acetaldehyde. Nevertheless, the data are consistent with the limited data on concentrations of acetaldehyde in drinking water in other countries.

Although there are data on concentrations of acetaldehyde in the vicinity of the largest industrial emitter in Canada, similar information is not available for other industrial sources, nor is the proximity of measured values to residential areas for the largest emitter known.

The degree of confidence in the database on toxicity that serves as the basis for the development of the tolerable concentration (TC) for inhalation is moderate, although there is a relatively high degree of confidence that critical effects occur at the initial site of exposure. Available data are considered inadequate to characterize dose–response for adverse effects following ingestion, and further study in this area is desirable. Studies in humans are extremely limited and, for inhalation, are restricted primarily to early investigations of subjective sensory irritation; there are no studies in which histopathological effects in the upper respiratory tract of humans exposed to acetaldehyde have been examined for comparison with the results of investigations in animals.

By far the greatest source of uncertainty in the health assessment, however, is the relative lack of information concerning the potential roles of cytotoxicity, proliferation and induction of DNA–protein cross-links in the carcinogenicity of this compound at high concentrations and the resulting inability to take both the genetic and tissue damage endpoints quantitatively into account in development of measures of dose–response relevant to the general population. Additional investigation in this area is warranted. However, it seems unlikely that this additional work will impact significantly on the priority for investigation of options to reduce exposure indicated here, which is only moderate.

The TC_{05} and TCL_{05} for the combined incidence of adenocarcinomas and squamous cell carcinomas developed in this assessment are approximately twofold higher than and the same as the TC_{05} and TCL_{05}, respectively, for adenocarcinomas alone and three- and sixfold less than the TC_{05} and TCL_{05}, respectively, for squamous cell carcinomas alone.

The measure of carcinogenic potency (TC_{05}) developed in this assessment was approximately 2.5 times less than a comparable value ($BMCL_{05}$) for non-cancer effects. While the midpoint estimate for a BMC for non-neoplastic effects developed on the basis of the less robust data in female rats was greater than that in males (basis of the BMC_{05} in this assessment), the lower 95% confidence limit was 13-fold less than the corresponding value for males. The lower 95% confidence limits for both the carcinogenic potency (TC_{05}) and measure of dose–response for non-cancer effects (BMC_{05}) developed in this assessment were at most threefold less than the midpoint estimates.

3.4 Conclusions

CEPA 1999 64(a): Based on available data, it has been concluded that acetaldehyde is not entering the environment in a quantity or concentration or under conditions that have or may

have an immediate or long-term harmful effect on the environment or its biological diversity. Therefore, acetaldehyde is not considered to be "toxic" as defined in Paragraph 64(a) of CEPA 1999.

CEPA 1999 64(b): Based on available data, it has been concluded that acetaldehyde is entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends. Therefore, acetaldehyde is considered to be "toxic" as defined in Paragraph 64(b) of CEPA 1999.

CEPA 1999 64(c): Although other factors may also play a role, there is a genetic component of the induction of tumours by inhalation of acetaldehyde. On this basis, acetaldehyde is considered to be "toxic" as defined in Paragraph 64(c) of CEPA 1999. For compounds where induction of cancer through direct interaction with genetic material cannot be ruled out, this approach is consistent with the objective that exposure be reduced wherever possible and obviates the need to establish an arbitrary "*de minimis*" level of risk for the determination of "toxic" under CEPA 1999. However, based on this approach and estimates of population exposure, the priority for investigation of options to reduce exposure for the general population in the ambient environment is considered to be moderate only, but high in the vicinity of an industrial point source.

Overall conclusion: Based on critical assessment of relevant information, acetaldehyde is considered to be "toxic" as defined in Section 64 of CEPA 1999.

3.5 Considerations for follow-up (further action)

Acetaldehyde may be important in the photochemical formation of ground-level ozone along with other reactive volatile organic chemicals. It is recommended that key sources of acetaldehyde be addressed, therefore, as part of management plans for volatile organic chemicals that contribute to the formation of ground-level ozone.

Based on the adopted approach to the assessment of the carcinogenicity of acetaldehyde and estimates of population exposure, the priority for investigation of options to reduce exposure in the general population in the ambient environment is considered to be moderate only. In general, therefore, investigation of options to reduce exposure in the context of CEPA is not considered a high priority and should be undertaken only if deemed appropriate in the context of other likely (higher) priorities for other PSL compounds, although additional work in the vicinity of industrial sources and on indoor air may be warranted.

Additional monitoring in residential areas in the vicinity of industrial sources is recommended, based on data collected in the vicinity of the largest emitter in Canada, which indicates that the priority for options to reduce exposure based on carcinogenic potency is high and the tolerable concentration for non-neoplastic effects is exceeded.

Concentrations of acetaldehyde in indoor air are consistently higher (by a factor of approximately 10-fold) than levels in ambient air. Available data are inadequate to determine the relative contribution of identified sources, such as consumer products, cigarette smoke, combustion appliances, building materials, cooking and infiltration of vehicle exhaust, although cigarette smoke appears to be important in this context. Identification of sources may be an area that deserves prioritization for further investigation.

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APPENDIX A SEARCH STRATEGIES EMPLOYED FOR IDENTIFICATION OF RELEVANT DATA

Environmental assessment

Data relevant to the assessment of whether acetaldehyde is "toxic" to the environment under CEPA were identified from existing review documents, published reference texts and on-line searches conducted between January and May 1996 of the following databases: Aqualine (Water Research Centre, Buckinghamshire; 1990–1996), ASFA (Aquatic Sciences and Fisheries Abstracts, Cambridge Scientific Abstracts; 1996), BIOSIS (Biosciences Information Services; 1990–1996), CAB (Commonwealth Agriculture Bureaux; 1990–1996), CESARS (Chemical Evaluation Search and Retrieval System, Ontario Ministry of the Environment and Michigan Department of Natural Resources; 1996), Chemical Abstracts (Chemical Abstracts Service, Columbus, Ohio; 1990–1996), CHRIS (Chemical Hazard Release Information System; 1964–1985), Current Contents (Institute for Scientific Information; 1990–1992, 1996), ELIAS (Environmental Library Integrated Automated System, Environment Canada library; January 1996), Enviroline (R.R. Bowker Publishing Co.; November 1995 – June 1996), Environmental Abstracts (1975 – February 1996), Environmental Bibliography (Environmental Studies Institute, International Academy at Santa Barbara; 1990–1996), GEOREF (Geo Reference Information System, American Geological Institute; 1990–1996), HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine; 1990–1996), Life Sciences (Cambridge Scientific Abstracts; 1990–1996), NTIS (National Technical Information Service, U.S. Department of Commerce; 1990–1996), Pollution Abstracts (Cambridge Scientific Abstracts, U.S. National Library of Medicine; 1990–1996), POLTOX (Cambridge Scientific Abstracts, U.S. National Library of Medicine; 1990–1995), RTECS (Registry of Toxic Effects of Chemical Substances, U.S. National Institute for Occupational Safety and Health; 1996), Toxline (U.S. National Library of Medicine; 1990–1996), TRI93 (Toxic Chemical Release Inventory, U.S. Environmental Protection Agency, Office of Toxic Substances; 1993), USEPA-ASTER (Assessment Tools for the Evaluation of Risk, U.S. Environmental Protection Agency; up to December 21, 1994), WASTEINFO (Waste Management Information Bureau of the American Energy Agency; 1973 – September 1995) and Water Resources Abstracts (U.S. Geological Survey, U.S. Department of the Interior; 1990–1996).

A survey of Canadian industry was carried out under authority of Section 16 of CEPA (Environment Canada, 1997d). Companies were required to provide information on uses, releases, environmental concentrations, effects or other data on acetaldehyde that were available to them if they met the trigger quantity of 1000 kg acetaldehyde per year. Reveal Alert was used to maintain an ongoing record of the current scientific literature pertaining to the potential environmental effects of acetaldehyde. Data obtained after January 1999 were not considered in this assessment unless they were critical data received during the 60-day public review of the report (August 14 to October 13, 1999).

Health assessment

Data relevant to the assessment of the potential risks of acetaldehyde to human health were identified through evaluation of existing review documents of the U.S. Environmental Protection Agency, Environmental Criteria Assessment Office (U.S. EPA, 1987), the International Programme on Chemical Safety (IPCS, 1995), the International Agency for Research on Cancer (IARC, 1985, 1987) and the Dutch Expert

Committee on Occupational Standards (DECOS, 1993), as well as a review prepared under contract for Health Canada (1996). A survey of Canadian industries was conducted under Section 16 of CEPA, in which companies were required to supply information concerning the use, release, environmental levels and toxicological effects of acetaldehyde (Environment Canada, 1997d). To identify additional relevant exposure and toxicological data, literature searches on acetaldehyde were conducted using the strategy of searching by its name or CAS registry number in the following databases: Canadian Research Index, CCRIS (Chemical Carcinogenesis Research Information System, U.S. National Cancer Institute), Dialog, EMIC (Environmental Mutagen Information Center database, Oak Ridge National Laboratory), GENE-TOX (Genetic Toxicology, Office of Toxic Substances, U.S. Environmental Protection Agency), HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine), IRIS (Integrated Risk Information System, U.S. Environmental Protection Agency) and RTECS (Registry of Toxic Effects of Chemical Substances, U.S. National Institute for Occupational Safety and Health). Its name, registry number and major synonyms were searched in the Toxline (U.S. National Library of Medicine; 1985–1998) and Medline (U.S. National Library of Medicine; 1989–1998) databases. The CAS registry number was searched in the Toxnet (1985–1997) database. The EMBASE database (on-line version of Excerpta Medica, Elsevier Science), from 1985 to 1997, was searched using the name, registry number and major synonyms. Only relevant toxicity data acquired prior to February 1998 and exposure data acquired prior to April 1998 were considered in the determination of whether acetaldehyde is "toxic" to human health.